STIC SDNsearch
July 2006
MLL 4/4/07

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=> d his ful

     (FILE 'REGISTRY' ENTERED AT 12:35:54 ON 13 JUL 2006)
                DEL HIS Y
L1              STR 84057-84-1
L2            26 SEA FAM FUL L1
                D SCAN
                E C9H7C12N5
                E C9H7C12N5/MF
                E C9H7CL2N5/MF
L3            69 SEA ABB=ON  PLU=ON  C9H7CL2N5.XCLH/MF OR C9H7CL2N5.CLH/MF OR
                C9H7CL2N5.BRH/MF OR C9H7CL2N5/MF
L4             3 SEA ABB=ON  PLU=ON  L3 AND L2
                D SCAN

     FILE 'CAPLUS' ENTERED AT 12:41:14 ON 13 JUL 2006
L5          1114 SEA ABB=ON  PLU=ON  L2
   L6       39538 SEA ABB=ON  PLU=ON  EPILEPSY/OBI OR ANTIEPILEP?/OBI OR
                CONVULS?/OBI OR ANTICONVUL?/OBI
L7         41971 SEA ABB=ON  PLU=ON  L6 OR SEIZURE?/OBI
L8           699 SEA ABB=ON  PLU=ON  L7 AND L5


     FILE 'CAPLUS' ENTERED AT 12:47:28 ON 13 JUL 2006
L9        211210 SEA ABB=ON  PLU=ON  MORPHOL?/OBI
L10       504660 SEA ABB=ON  PLU=ON  PARTICLE?/OBI
L11       145393 SEA ABB=ON  PLU=ON  (SURFACE (3A) AREA)/BI
L12            6 SEA ABB=ON  PLU=ON  L8 AND L9
L13            4 SEA ABB=ON  PLU=ON  L8 AND L10
L14            3 SEA ABB=ON  PLU=ON  L8 AND L11
L15       159110 SEA ABB=ON  PLU=ON  DRUG DELIVE?/OBI
L16           63 SEA ABB=ON  PLU=ON  L8 AND L15
L17         3486 SEA ABB=ON  PLU=ON  EXCIPIENT?/OBI
L18            2 SEA ABB=ON  PLU=ON  L17 AND L8
L19        12564 SEA ABB=ON  PLU=ON  EXCIPIENT?/BI
L20            5 SEA ABB=ON  PLU=ON  L8 AND L19
L21       450154 SEA ABB=ON  PLU=ON  MORPHOL?/BI
L22      1177796 SEA ABB=ON  PLU=ON  PARTICLE?/BI
L23           15 SEA ABB=ON  PLU=ON  L8 AND (L22 OR L21 )
L24         1347 SEA ABB=ON  PLU=ON  TONICITY?/BI

     FILE 'REGISTRY' ENTERED AT 12:50:35 ON 13 JUL 2006
                E DEXTROSE
                E DEXTROSE/CN
L25            1 SEA ABB=ON  PLU=ON  DEXTROSE/CN

     FILE 'CAPLUS' ENTERED AT 12:50:46 ON 13 JUL 2006
L26       191485 SEA ABB=ON  PLU=ON  L25 OR DEXTROSE/OBI
L27            9 SEA ABB=ON  PLU=ON  L8 AND L26
L28            0 SEA ABB=ON  PLU=ON  L8 AND L24
L29           24 SEA ABB=ON  PLU=ON  (L12 OR L13 OR L14) OR L18 OR L20 OR L23
                OR L27
L30           10 SEA ABB=ON  PLU=ON  CARRIER/OBI AND L8
L31           31 SEA ABB=ON  PLU=ON  L30 OR L29
L32           74 SEA ABB=ON  PLU=ON  ARONHIME J?/AU
L33            6 SEA ABB=ON  PLU=ON  SAMBURSKI G?/AU
L34           78 SEA ABB=ON  PLU=ON  (L32 OR L33)
L35            2 SEA ABB=ON  PLU=ON  L34 AND L5
L36            0 SEA ABB=ON  PLU=ON  L35 NOT L31
L37           12 SEA ABB=ON  PLU=ON  L5 AND L21
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L38             4 SEA ABB=ON  PLU=ON  L37 NOT L31
                  D SCAN TI
L39        341291 SEA ABB=ON  PLU=ON  ((XRAY OR X RAY)(L) DIFFRACT?)/BI
L40             2 SEA ABB=ON  PLU=ON  L39 AND L5
L41       1286897 SEA ABB=ON  PLU=ON  CRYST?/OBI
L42            11 SEA ABB=ON  PLU=ON  L5 AND L41
L43            11 SEA ABB=ON  PLU=ON  L40 OR L42
L44            10 SEA ABB=ON  PLU=ON  L43 NOT L31
L45            75 SEA ABB=ON  PLU=ON  ARONHIME J?/AU
L46             6 SEA ABB=ON  PLU=ON  SAMBURSKI G?/AU
L47            79 SEA ABB=ON  PLU=ON  L45 OR L46
L48             2 SEA ABB=ON  PLU=ON  L5 AND L47

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:58:32 ON 13 JUL 2006
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provided by InfoChem.

STRUCTURE FILE UPDATES:   12 JUL 2006  HIGHEST RN 892389-74-1
DICTIONARY FILE UPDATES:  12 JUL 2006  HIGHEST RN 892389-74-1

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d que stat l2
L1                STR
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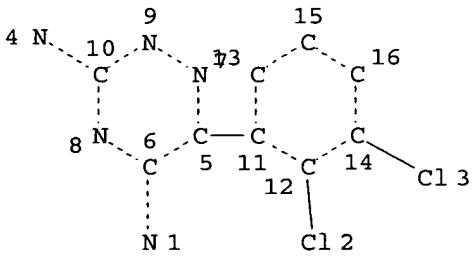


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16
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STEREO ATTRIBUTES: NONE
L2            26 SEA FILE=REGISTRY FAM FUL L1

100.0% PROCESSED      51 ITERATIONS                          26 ANSWERS
SEARCH TIME: 00.00.01


=> fil  caplus
FILE 'CAPLUS' ENTERED AT 12:58:48 ON 13 JUL 2006
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FILE COVERS 1907 - 13 Jul 2006  VOL 145 ISS 3
FILE LAST UPDATED: 12 Jul 2006  (20060712/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos l31
L1             STR
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L5          1114 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L6         39538 SEA FILE=CAPLUS ABB=ON  PLU=ON  EPILEPSY/OBI OR ANTIEPILEP?/OBI
                  OR CONVULS?/OBI OR ANTICONVUL?/OBI
L7         41971 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 OR SEIZURE?/OBI
L8           699 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND L5
L9        211210 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/OBI
L10       504660 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/OBI
L11       145393 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SURFACE (3A) AREA)/BI
L12            6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L9
L13            4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L10
L14            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L11
L17         3486 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/OBI
L18            2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17 AND L8
L19        12564 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/BI
L20            5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L19
L21       450154 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/BI
L22      1177796 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/BI
L23           15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L22 OR L21 )
L25            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DEXTROSE/CN
L26       191485 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25 OR DEXTROSE/OBI
L27            9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L26
L29           24 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L12 OR L13 OR L14) OR L18 OR
                  L20 OR L23 OR L27
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L30          10 SEA FILE=CAPLUS ABB=ON  PLU=ON  CARRIER/OBI AND L8
L31          31 SEA FILE=CAPLUS ABB=ON  PLU=ON  L30 OR L29


=> d que nos l38
L1              STR
L2           26 SEA FILE=REGISTRY FAM FUL L1
L5         1114 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L6        39538 SEA FILE=CAPLUS ABB=ON  PLU=ON  EPILEPSY/OBI OR ANTIEPILEP?/OBI
                 OR CONVULS?/OBI OR ANTICONVUL?/OBI
L7        41971 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 OR SEIZURE?/OBI
L8          699 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND L5
L9       211210 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/OBI
L10      504660 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/OBI
L11      145393 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SURFACE (3A) AREA)/BI
L12           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L9
L13           4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L10
L14           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L11
L17        3486 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/OBI
L18           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17 AND L8
L19       12564 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/BI
L20           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L19
L21      450154 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/BI
L22     1177796 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/BI
L23          15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L22 OR L21 )
L25           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DEXTROSE/CN
L26      191485 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25 OR DEXTROSE/OBI
L27           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L26
L29          24 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L12 OR L13 OR L14) OR L18 OR
                 L20 OR L23 OR L27
L30          10 SEA FILE=CAPLUS ABB=ON  PLU=ON  CARRIER/OBI AND L8
L31          31 SEA FILE=CAPLUS ABB=ON  PLU=ON  L30 OR L29
L37          12 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 AND L21
L38           4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L37 NOT L31


=> d que nos l44
L1              STR
L2           26 SEA FILE=REGISTRY FAM FUL L1
L5         1114 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L6        39538 SEA FILE=CAPLUS ABB=ON  PLU=ON  EPILEPSY/OBI OR ANTIEPILEP?/OBI
                 OR CONVULS?/OBI OR ANTICONVUL?/OBI
L7        41971 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 OR SEIZURE?/OBI
L8          699 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND L5
L9       211210 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/OBI
L10      504660 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/OBI
L11      145393 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SURFACE (3A) AREA)/BI
L12           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L9
L13           4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L10
L14           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L11
L17        3486 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/OBI
L18           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17 AND L8
L19       12564 SEA FILE=CAPLUS ABB=ON  PLU=ON  EXCIPIENT?/BI
L20           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L19
L21      450154 SEA FILE=CAPLUS ABB=ON  PLU=ON  MORPHOL?/BI
L22     1177796 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARTICLE?/BI
L23          15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L22 OR L21 )
L25           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DEXTROSE/CN
L26      191485 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25 OR DEXTROSE/OBI
L27           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L26
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L29          24 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L12 OR L13 OR L14) OR L18 OR
                L20 OR L23 OR L27
L30          10 SEA FILE=CAPLUS ABB=ON  PLU=ON  CARRIER/OBI AND L8
L31          31 SEA FILE=CAPLUS ABB=ON  PLU=ON  L30 OR L29
L39      341291 SEA FILE=CAPLUS ABB=ON  PLU=ON  ((XRAY OR X RAY)(L) DIFFRACT?)/
                BI
L40           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L39 AND L5
L41     1286897 SEA FILE=CAPLUS ABB=ON  PLU=ON  CRYST?/OBI
L42          11 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 AND L41
L43          11 SEA FILE=CAPLUS ABB=ON  PLU=ON  L40 OR L42
L44          10 SEA FILE=CAPLUS ABB=ON  PLU=ON  L43 NOT L31

=> d que nos l48          Inventor search

L45          75 SEA FILE=CAPLUS ABB=ON  PLU=ON  ARONHIME J?/AU
L46           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  SAMBURSKI G?/AU
L47          79 SEA FILE=CAPLUS ABB=ON  PLU=ON  L45 OR L46
L1              STR
L2           26 SEA FILE=REGISTRY FAM FUL L1
L5         1114 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L7            2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 AND L47


=> d .ca l31 1-31;d .ca l38 1-4; d .ca l44 1-10; d ibib l48 1-2

L31  ANSWER 1 OF 31  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:340351  CAPLUS
DOCUMENT NUMBER:          144:390947
TITLE:                    Preparation of sulfamoylbenzamides as agonists of
                          cannabinoid receptors
INVENTOR(S):              Dolle, Roland E.; Worm, Karin; Zhou, Q. Jean
PATENT ASSIGNEE(S):       Adolor Corporation, USA
SOURCE:                   U.S. Pat. Appl. Publ., 130 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 2006079557         A1    20060413    US 2005-251160           20051013
     WO 2006044645         A2    20060427    WO 2005-US36997          20051012
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
             NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
             SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
             YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       US 2004-618387P     P  20041013
ED   Entered STN:  13 Apr 2006
GI
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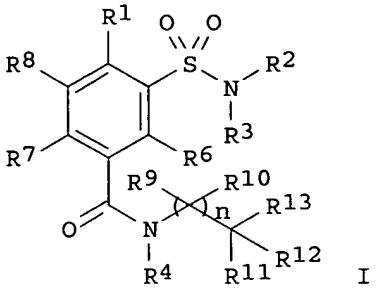

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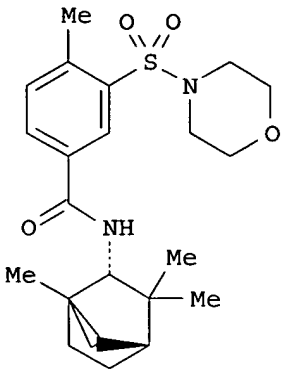


II

AB The title sulfamoylbenzamides I [wherein n = 0-3; R1 = H, F, Cl, Br, (cyclo)alkyl, (hetero)aryl, (hetero)aralkyl, etc.; R2 and R3 = independently H, (cyclo)alkyl, (hetero)aryl, (hetero)aralkyl, etc.; or R2 and R3 form a ring; R4 = H or alkyl; R6-R8 = independently H, F, Cl, Br, or alkyl; R9-R11 = independently H or alkyl; R12 and R13 form a ring; with provisos], or pharmaceutically acceptable salts thereof were prepared as agonists of cannabinoid (CB) receptors. For example, II was prepared in a multi-step synthesis. II showed agonistic activity with EC50 = 2003 and 7.8 nM against human cloned CB1 and CB2 receptors, resp. The compds. are useful for treating and/or preventing pain, gastrointestinal disorders, inflammation, immune diseases, ischemic conditions, etc. (no data).

INCL 514317000; 514602000; 514319000; 546205000; 564086000

CC 28-18 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 25, 63

ST prepn sulfamoylbenzamide **morpholine** agonist cannabinoid receptor human; treatment pain inflammation immune ischemia asthma disease

IT Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarrhythmics
Antiasthmatics
Anticonvulsants
Antidiabetic agents
Antidiarrheals
Antiemetics
Antihypertensives
Antimigraine agents
Antiosteoporotic agents
Antiparkinsonian agents
Antirheumatic agents
Apoptosis
Asthma
Autoimmune disease
Cachexia
Celiac disease
Diarrhea
Digestive tract, disease

Eating disorders
Emphysema
Gastrointestinal agents
Human
Hypertension
Immune disease
Immunosuppressants
Inflammation
Ischemia
Mental and behavioral disorders
Multiple sclerosis
Myasthenia gravis
Nausea
Nervous system, disease
Nervous system agents
Nervous system depressants
Osteoporosis
Pain
Parkinson's disease
Psoriasis
Reperfusion
Rheumatoid arthritis
Seizures
Sjogren syndrome
Transplant rejection
Vomiting
(preparation of sulfamoylbenzamides as agonists of cannabinoid receptors)

IT 50-48-6 50-78-2 57-27-2, biological studies 57-41-0 57-42-1 59-92-7, biological studies 76-41-5 76-42-6 76-57-3 76-99-3 77-07-6 103-90-2 125-28-0 125-29-1 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 359-83-1 437-38-7 466-99-9 469-62-5 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 2323-36-6 13956-29-1 15686-91-6 20594-83-6 22204-53-1 27203-92-5, Tramadol 28860-95-9 42408-82-2 51146-56-6 52485-79-7 53179-11-6 53648-55-8 56030-54-7 60142-96-3 71195-58-9 **84057-84-1** 107447-28-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug candidate; preparation of sulfamoylbenzamides as agonists of cannabinoid receptors)

IT 62-53-3, Phenylamine, reactions 74-11-3, 4-Chloro benzoic acid 74-89-5, Methylamine, reactions 96-32-2, Bromoacetic acid methyl ester 98-80-6, Phenyl boronic acid 99-94-5, 4-Methyl benzoic acid 100-46-9D, Benzylamine, resin bound 103-67-3, N-Methylbenzylamine 103-67-3D, N-Methyl-N-benzylamine, resin bound 108-18-9 109-90-0, Ethyl isocyanate 110-89-4, Piperidine, reactions 110-91-8, **Morpholine**, reactions 123-75-1, Pyrrolidine, reactions 124-40-3, N,N-Dimethylamine, reactions 141-91-3, 2,6-Dimethylmorpholine 496-12-8, 1,3-DihydroIsoindole 503-29-7, Azetidine 586-76-5, 4-Bromobenzoic acid 627-41-8 635-46-1 2051-28-7 2548-29-0 2799-21-5 3367-95-1, N,N-Diethylpiperidine-3-carboxamide 3731-52-0D, 3-Pyridinemethylamine, resin bound 3850-30-4 4025-64-3 5006-62-2, Ethyl piperidine-3-carboxylate 5071-96-5D, 3-Methoxybenzylamine, resin bound 5382-16-1, 4-Hydroxypiperidine 5813-64-9 5813-64-9D, resin bound 13074-39-0, Adamantan-2-amine 13293-47-5 13392-28-4 13889-98-0, N-Acetylpiperazine 15901-42-5 17768-41-1, Tricyclo[3.3.1.13,7]decane-1-methanamine 35794-11-7, 3,5-Dimethylpiperidine 38256-93-8, N-Methyl-2-methoxyethylamine 51942-56-4 57260-71-6, N-tert-Butoxycarbonylpiperazine 59815-29-1 69460-11-3 73522-42-6 90812-24-1 100243-39-8, (S)-3-Hydroxypyrrolidine 116574-75-5, 3-Fluoropiperidine 131348-01-1 151104-64-2 165883-10-3D, resin bound 191483-49-5 264927-50-6

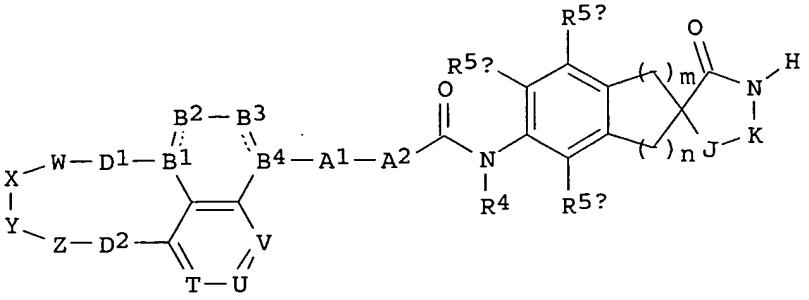
313346-23-5 500596-03-2 591781-14-5 847798-58-7 883145-58-2
883145-59-3 883145-60-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfamoylbenzamides as agonists of cannabinoid receptors)

L31 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:269581 CAPLUS
DOCUMENT NUMBER: 144:312071
TITLE: Preparation of tricyclic anilide spirolactam CGRP receptor antagonists
INVENTOR(S): Bell, Ian M.; Gallicchio, Steven N.; Stump, Craig A.; Theberge, Cory R.; Vacca, Joseph P.; Zartman, C. Blair; Zhang, Xufang
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006031491	A2	20060323	WO 2005-US31617	20050906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-608294P P 20040909
OTHER SOURCE(S): MARPAT 144:312071
ED Entered STN: 23 Mar 2006
GI



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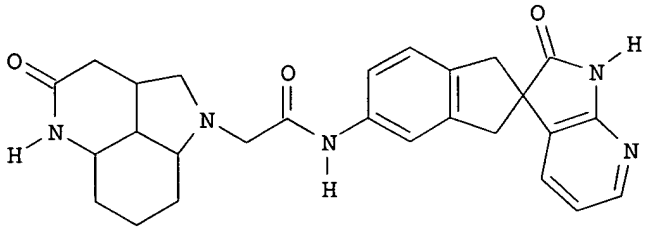

II

AB Title compds. I [A1 and A2 independently = bond or CR13R14, where one of A1 and A2 is optionally absent; B1 and B4 independently = C when double bond present, CR1 or N; B2 and B3 independently = bond, CR1R2, CO, CS, O, S, etc., where one of B2 and B3 is optionally absent; D1 and D2 independently = O, S, SO2, CR1R2, CO, etc.; J = =C(R6a)-; CR13R14, and CO; K = =C(R6b), CR13R14, CO, etc.; T, U and V independently = =C(R1)- and =N-, wherein at least one of T, U, and V = =C(R1)-; W, X, Y, and Z = bond, CR1R2, CS, O, etc.; R1 and R2 = H, (un)substituted alkyl, cycloalkyl, alkynyl, etc.; R4 = H, (un)substituted alkyl, benzyl, etc.; R5a, R5b, and R5c = H, alkyl, alkoxy, halo, etc.; R6a = H, OH, halo, CN, (un)substituted alkyl, etc.; R13 and R14 = H, OH, halo, and (un)substituted alkyl; m = 1 or 2; n = 1 or 2], and their pharmaceutically acceptable salts, useful as antagonists of calcitonin gene-related peptide (CGRP) receptors and useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. Thus, e.g., II was prepared by reaction of (-)-5-amino-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'H)-one (preparation given) with lithium (4-oxo-2a,3,4,5-tetrahydropyrrolo[4,3,2-de]quinolin-1(2H)-yl)acetate (preparation given). I demonstrated activity as antagonists of the CGRP receptor with Ki or IC50 values generally less than about 50 μM. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT Drug delivery systems
(**carriers**; tricyclic anilide spirolactam compds. as CGRP antagonists useful in prevention and treatment of such diseases in which CGRP is involved)

IT 5-HT agonists
Analgesics
Anti-inflammatory agents
Anticonvulsants
Antihypertensives

Antimigraine agents
Combination chemotherapy
Headache
Human
(tricyclic anilide spirolactam compds. as CGRP antagonists useful in prevention and treatment of such diseases in which CGRP is involved)

IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 53-86-1, Indomethacin 61-68-7, Mefenamic acid 103-90-2, Acetaminophen 113-15-5, Ergotamine 129-20-4, Oxyphenbutazone 511-12-6, Dihydroergotamine 530-78-9, Flufenamic acid 552-94-3, Salsalate 599-79-1, Sulfasalazine 644-62-2, Meclofenamic acid 13539-59-8, Apazone 13710-19-5, Tolfenamic acid 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 21256-18-8, Oxaprozin 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal 26171-23-3, Tolmetin 29679-58-1, Fenoprofen 36322-90-4, Piroxicam 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 51803-78-2, Nimesulide 59804-37-4, Tenoxicam 60142-96-3, Gabapentin 68291-97-4, Zonisamide 70374-39-9, Lornoxicam 71125-38-7, Meloxicam 74103-06-3, Ketorolac 76584-70-8, Divalproex sodium **84057-84-1**, Lamotrigine 93384-43-1, Botulinum toxin A 93384-44-2, Botulinum toxin B 97240-79-4, Topiramate 102767-28-2, Levetiracetam 103628-46-2, Sumatriptan 115103-54-3, Tiagabine 120210-48-2, Tenidap 121679-13-8, Naratriptan 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan 144034-80-0, Rizatriptan 148553-50-8, Pregabalin 151140-96-4, Avitriptan 154323-57-6, Almotriptan 158747-02-5, Frovatriptan 182563-08-2, LY334370 185243-69-0, Etanercept 187665-65-2, PNU-142633
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances for use in combination chemotherapy with tricyclic anilide spirolactam compds. in treatment of diseases in which CGRP is involved)

L31 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:269508 CAPLUS
DOCUMENT NUMBER: 144:331420
TITLE: Preparation of bicyclic anilide spirolactam cgrp receptor antagonists
INVENTOR(S): Bell, Ian M.; Theberge, Cory R.; Stump, Craig A.; Zhang, Xufang; Gallicchio, Steven N.; Zartman, C. Blair
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006031610	A2	20060323	WO 2005-US32041	20050909

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-609292P P 20040913
OTHER SOURCE(S): MARPAT 144:331420
ED Entered STN: 23 Mar 2006

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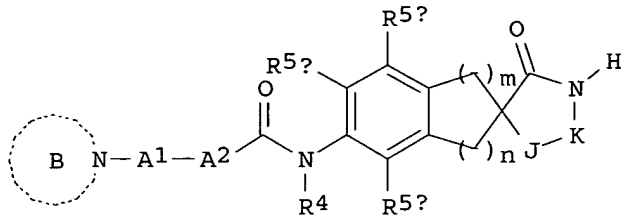

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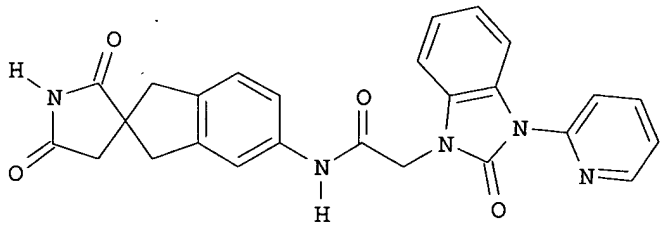

II

AB Title compds. I [A1 and A2 independently = bond or CR13R14, where one of A1 and A2 is optionally absent; B = (un)substituted bicycloheterocycle; J = =C(R6a)-; CR13R14, and CO; K = =C(R6b), CR13R14, CO, etc.; R4 = H, (un)substituted alkyl, benzyl, etc.; R5a, R5b, and R5c = H, alkyl, alkoxy, halo, etc.; R6a and R6b independently = H, OH, halo, (un)substituted alkyl, etc.; R13 and R14 = H or (un)substituted alkyl; m = 1 or 2; n = 1 or 2], and their pharmaceutically acceptable salts, useful as antagonists of calcitonin gene-related peptide (CGRP) receptors and useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. Thus, e.g., II was prepared by reaction of 5-amino-1,3-dihydro-2'H,5'H-spiro[indene-2,3'-pyrrolidine]-2',5'-dione (preparation given) with 5-amino-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'H)-one (preparation given). I demonstrated activity as antagonists of the CGRP receptor with Ki or IC50 values generally less than about 50 μM. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT Drug delivery systems
(**carriers**; preparation of bicyclic anilide spirolactam cgrp receptor antagonists)

IT 5-HT agonists
5-HT reuptake inhibitors
Analgesics
Anti-inflammatory agents

Anticonvulsants
Antidepressants
Antiemetics
Antihypertensives
Antipsychotics
Anxiolytics
Calcium channel blockers
Leukotriene antagonists
Prokinetic agents
Tranquilizers
(substances for use in combination chemotherapy with bicyclic anilide spirolactam compds. in prevention and treatment of diseases associated with CGRP receptor)

IT 50-33-9, Phenylbutazone, biological studies 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 50-53-3, biological studies 50-78-2, Aspirin 52-53-9, Verapamil 53-86-1, Indomethacin 58-25-3, Chlorodiazepoxide 58-38-8 61-68-7, Mefenamic acid 72-69-5, Nortriptyline 103-90-2, Acetaminophen 113-15-5, Ergotamine 129-20-4, Oxyphenbutazone 303-49-1, Clomipramine 438-60-8, Protriptyline 439-14-5, Diazepam 511-12-6, Dihydroergotamine 525-66-6, Propranolol 530-78-9, Flufenamic acid 548-73-2, Droperidol 552-94-3, Salsalate 599-79-1, Sulfasalazine 644-62-2, Meclofenamic acid 739-71-9, Trimipramine 1668-19-5, Doxepin 13539-59-8, Apazone 13710-19-5, Tolfenamic acid 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal 25775-90-0, Civamide 26171-23-3, Tolmetin 26839-75-8, Timolol 28981-97-7, Alprazolam 29122-68-7, Atenolol 29679-58-1, Fenoprofen 36322-90-4, Piroxicam 38194-50-2, Sulindac 41340-25-4, Etodolac 42200-33-9, Nadolol 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51384-51-1, Metoprolol 51803-78-2, Nimesulide 52468-60-7, Flunarizine 54910-89-3, Fluoxetine 59729-33-8, Citalopram 59804-37-4, Tenoxicam 60142-96-3, Gabapentin 61869-08-7, Paroxetine 62571-86-2, Captopril 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 68291-97-4, Zonisamide 70374-39-9, Lornoxicam 71125-38-7, Meloxicam 72509-76-3, Felodipine 74103-06-3, Ketorolac 75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 79617-96-2, Sertraline 82834-16-0, Perindopril **84057-84-1**, Lamotrigine 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 93384-43-1, Botulinum toxin A 93384-44-2, Botulinum toxin B 93413-69-5, Venlafaxine 97240-79-4, Topiramate 101477-55-8, Lomerizine 102767-28-2, Levetiracetam 103628-46-2, Sumatriptan 107753-78-6, Zafirlukast 111974-69-7, Quetiapine 114798-26-4, Losartan 115103-54-3, Tiagabine 116539-59-4, Duloxetine 120210-48-2, Tenidap 121679-13-8, Naratriptan 128196-01-0, Escitalopram 132539-06-1, Olanzapine 133040-01-4, Eprosartan 137862-53-4, Valsartan 138402-11-6, Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 143322-58-1, Eletriptan 144034-80-0, Rizatriptan 144689-24-7, Olmesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 148553-50-8, Pregabalin 151140-96-4, Avitriptan 154323-57-6, Almotriptan 158747-02-5, Frovatriptan 158966-92-8, Montelukast 182563-08-2, LY334370 185243-69-0, Etanercept 187665-65-2, PNU-142633
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances for use in combination chemotherapy with bicyclic anilide spirolactam compds. in prevention and treatment of diseases associated with CGRP receptor)

L31 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:268948 CAPLUS
DOCUMENT NUMBER: 144:331434
TITLE: Preparation of tricyclic anilide spirohydantoin CGRP receptor antagonists
INVENTOR(S): Bell, Ian M.; Gallicchio, Steven N.; Zartman, C. Blair; Theberge, Cory R.; Zhang, Xufang
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006031676	A2	20060323	WO 2005-US32288	20050909

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-609294P P 20040913
OTHER SOURCE(S): MARPAT 144:331434
ED Entered STN: 23 Mar 2006
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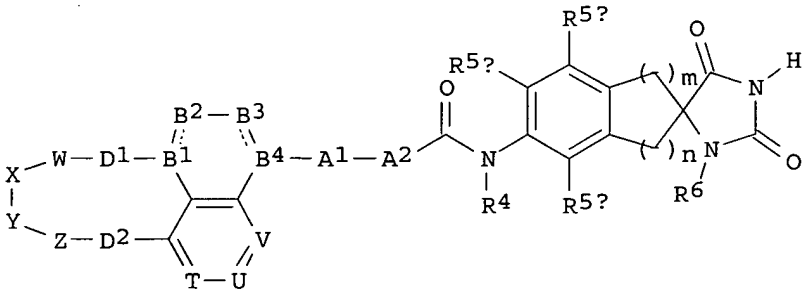

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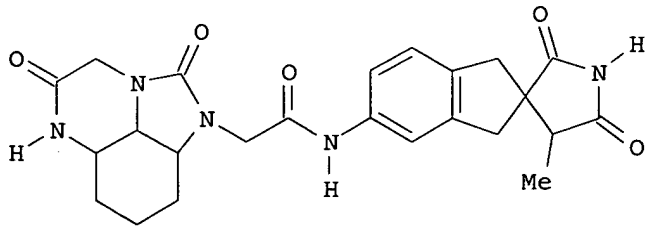

II

AB Title compds. I [A1 and A2 independently = bond or CR13R14, where one of A1 and A2 is optionally absent; B1 and B4 independently = C when double bond present, CR1 or N; B2 and B3 independently = bond, CR1R2, CO, CS, O, S, etc., where one of B2 and B3 is optionally absent; D1 and D2 independently = O, S, SO2, CR1R2, CO, etc.; T, U and V independently = =C(R1)- and =N-, wherein at least one of T, U, and V = =C(R1)-; W, X, Y, and Z = bond, CR1R2, CS, O, etc.; R1 and R2 = H, (un)substituted alkyl, cycloalkyl, alkynyl, etc.; R4 = H, (un)substituted alkyl, benzyl, etc.; R5a, R5b, and R5c = H, alkyl, alkoxy, halo, etc.; R6 = H, (un)substituted alkyl, cycloalkyl, etc.; R13 and R14 = H, OH, halo, and (un)substituted alkyl; m = 1 or 2; n = 1 or 2], and their pharmaceutically acceptable salts, useful as antagonists of calcitonin gene-related peptide (CGRP) receptors and useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. Thus, e.g., II was prepared by reaction of (-)-5'-amino-3-methylspiro[imidazolidine-4,2'-indane]-2,5-dione (preparation given) with sodium (2,5-dioxo-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-1(2H)yl)acetate (preparation given). I demonstrated activity as antagonists of the CGRP receptor with Ki or IC50 values generally less than about 50 μM. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT Drug delivery systems
(carriers; tricyclic anilide spirolactam compds. as CGRP antagonists useful in prevention and treatment of such diseases in which CGRP is involved)

IT 5-HT agonists
Analgesics
Anti-inflammatory agents
Anticonvulsants
Antihypertensives
Antimigraine agents
Combination chemotherapy
Headache
Human
(tricyclic anilide spirolactam compds. as CGRP antagonists useful in prevention and treatment of such diseases in which CGRP is involved)

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63675-72-9, Nisoldipine 66085-59-4, Nimodipine 68291-97-4, Zonisamide 70374-39-9, Lornoxicam 71125-38-7, Meloxicam 72509-76-3, Felodipine 74103-06-3, Ketorolac 75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 79617-96-2, Sertraline 82834-16-0, Perindopril **84057-84-1**, Lamotrigine 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 93384-43-1, Botulinum toxin A 93384-44-2, Botulinum toxin B 93413-69-5, Venlafaxine 97240-79-4, Topiramate 101477-55-8, Lomerizine 102767-28-2, Levetiracetam 103628-46-2, Sumatriptan 107753-78-6, Zafirlukast 111974-69-7, Quetiapine 114798-26-4, Losartan 115103-54-3, Tiagabine 116539-59-4, Duloxetine 120210-48-2, Tenidap 121679-13-8, Naratriptan 128196-01-0, Escitalopram 132539-06-1, Olanzapine 133040-01-4, Eprosartan 137862-53-4, Valsartan 138402-11-6, Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 143322-58-1, Eletriptan 144034-80-0, Rizatriptan 144689-24-7, Olmesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 148553-50-8, Pregabalin 151140-96-4, Avitriptan 154323-57-6, Almotriptan 158747-02-5, Frovatriptan 158966-92-8, Montelukast 182563-08-2, LY334370 185243-69-0, Etanercept 187665-65-2, PNU-142633
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances for use in combination chemotherapy with tricyclic anilide spirolactam compds. in prevention and treatment of diseases associated with CGRP receptor)

L31 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:152711 CAPLUS
DOCUMENT NUMBER: 144:226261
TITLE: Alpha-ketoglutarates and their use as therapeutic agents for the treatment of cancer and other disorders
INVENTOR(S): Gottlieb, Eyal; Selak, Mary A.; Mackenzie, Elaine D.; Watson, David G.
PATENT ASSIGNEE(S): Cancer Research Technology Limited, UK
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016143	A1	20060216	WO 2005-GB3119	20050809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2004-17715 A 20040809
GB 2004-21921 A 20041001
OTHER SOURCE(S): MARPAT 144:226261

ED Entered STN: 17 Feb 2006

AB The present invention relates to α-ketoglutarates of general formula R2OCOCH2CH2COOR1 (wherein R1 and R2 = H or a hydrophobic moiety; with the proviso that R1 and R2 are not both H) and pharmaceutically acceptable salts, solvates, amides, esters, ethers, N-oxides, chemical protected forms, and prodrugs thereof. These compds. activate HIFα hydroxylase or prolyl hydroxylase or increase the level of α-ketoglutarate and are useful in the treatment of cancer (e.g., cancer in which the activity of one of the enzymes in the tricarboxylic acid (TCA) cycle is down regulated) or in the treatment of angiogenesis (e.g., hypoxia-induced angiogenesis).

IC ICM C07C069-716
ICS C07D311-72; A61K031-225; A61P035-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 23, 25, 27

IT **Anticonvulsants**
(addnl. therapeutic agents; alpha-ketoglutarates and their use as therapeutic agents for treatment of cancer and other disorders in combination with other agents)

IT 50-06-6, Phenobarbital, biological studies 50-18-0, Cyclophosphamide 50-78-2, Aspirin 50-81-7, Ascorbic Acid, biological studies **50-99-7**, D-Glucose, biological studies 52-28-8 54-05-7, Chloroquine 56-75-7, Chloramphenicol 57-41-0, Phenytoin 57-48-7, Fructose, biological studies 58-15-1, Amidopyrine 58-95-7, α-Tocopherol acetate 59-30-3, Folic Acid, biological studies 64-17-5, Ethanol, biological studies 65-23-6, Pyridoxine 68-89-3, Dipyrone 69-53-4, Ampicillin 70-51-9, Deferoxamine 77-41-8, Methsuximide 77-67-8, Ethosuximide 80-08-0, Dapsone 86-34-0, Phensuximide 98-96-4, Pyrazinamide 103-90-2, Paracetamol 114-07-8, Erythromycin 115-67-3, Paramethadione 123-56-8D, Succinimide, derivs. 125-28-0, Dihydrocodeine 125-33-7, Primidone 126-07-8, Griseofulvin 129-20-4, Oxyphenbutazone 298-46-4, Carbamazepine 299-78-5, Allylisopropylacetamide 379-79-3, Ergotamine Tartrate 439-14-5, Diazepam 461-72-3D, Hydantoin, derivs. 479-92-5, Propyphenazone 480-30-8, Dichloralphenazone 514-78-3, Canthaxanthin 1404-90-6, Vancomycin 5250-39-5, Flucloxacillin 6190-39-2, Dihydroergotamine-Mesylate 7235-40-7, β Carotene 7439-89-6, Iron, biological studies 7440-43-9, Cadmium, biological studies 13539-59-8, Azapropazone 15307-79-6, Diclofenac sodium 25451-15-4, Felbamate 29094-61-9, Glipizide 51568-18-4, Succinylacetone 79236-56-9, N-Methylprotoporphyrin IX **84057-84-1**, Lamotrigine 100438-92-4, Heme arginate 115103-54-3, Tiagabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agents; alpha-ketoglutarates and their use as therapeutic agents for treatment of cancer and other disorders in combination with other agents)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1356150 CAPLUS
DOCUMENT NUMBER: 145:770
TITLE: Toxic epidermal necrolysis with combination lamotrigine and valproate in bipolar disorder
AUTHOR(S): Chang, Chuan-Chia; Shiah, I-Shin; Chang, Hsin-An; Huang, San-Yuan
CORPORATE SOURCE: Department of Psychiatry, Tri-Service General Hospital, Taipei, Taiwan
SOURCE: Progress in Neuro-Psychopharmacology & Biological

Psychiatry (2006), 30(1), 147-150
CODEN: PNPPD7; ISSN: 0278-5846
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Dec 2005
AB Toxic epidermal necrolysis (TEN) is the most severe and potentially life-threatening cutaneous reaction associated with lamotrigine. The risk of developing TEN during lamotrigine therapy is low and previously reported cases most involved epileptic patients. However, the risk of TEN with combination lamotrigine and valproate is greater than with monotherapy. We present here the emergence of TEN in a 32-yr-old bipolar woman who was concomitantly treated with lamotrigine and valproate. The patient developed high fever, pharyngitis, cervical lymphadenopathy, mucosal sloughing, generalized erythematous eruptions and more than 40% epidermal detachment of the total body **surface area** (TBSA) after we added lamotrigine to her medications of valproate and trazodone. The patient's illness course was protracted and accompanied with hepatitis, pneumonitis and hematol. abnormalities. In the beginning of her illness course, our patient did not respond to antihistamine treatment. However, she made a full recovery without any sequela after she had received systemic corticosteroid and intensive resuscitation. Our case suggests that early use of systemic corticosteroid might be beneficial in treating TEN patients, if there is not any clin. contraindication.
CC 1-11 (Pharmacology)
IT **Anticonvulsants**
(emergence of toxic epidermal necrolysis was observed with **anticonvulsant** lamotrigine and valproate treatment while systemic corticosteroid and intensive resuscitation made full recovery without sequela in patient with bipolar II depression)
IT 99-66-1 **84057-84-1**, Lamotrigine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emergence of toxic epidermal necrolysis was observed with combined lamotrigine and valproate treatment while systemic corticosteroid and intensive resuscitation made full recovery without any sequela in patient with bipolar II depression)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1290048 CAPLUS
DOCUMENT NUMBER: 144:17195
TITLE: Treating **seizures** using ice inhibitors
INVENTOR(S): Vezzani, Annamaria; Randle, John C. R.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115362	A1	20051208	WO 2005-US17177	20050516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,

NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2006128696 A1 20060615 US 2005-130659 20050516
PRIORITY APPLN. INFO.: US 2004-571314P P 20040515
ED Entered STN: 09 Dec 2005
AB The invention relates to methods and compns. for treating or preventing seizures.
IC ICM A61K031-00
ICS A61K031-551; A61K031-4025; A61K031-40; A61P025-08
CC 1-11 (Pharmacology)
ST caspase ICE inhibitor pharmaceutical **anticonvulsant** **epilepsy** combination therapy
IT **Anticonvulsants**
Combination chemotherapy
Convulsion
Epilepsy
Human
Seizures
(ICE inhibitors for treatment and prevention of **seizures**)
IT Interleukin 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICE inhibitors for treatment and prevention of **seizures**)
IT Drug delivery systems
(**carriers**; ICE inhibitors for treatment and prevention of **seizures**)
IT Brain
(hippocampus; ICE inhibitors for treatment and prevention of **seizures**)
IT Drug delivery systems
(intracranial; ICE inhibitors for treatment and prevention of **seizures**)
IT Drug delivery systems
(oral; ICE inhibitors for treatment and prevention of **seizures**)
IT Drug delivery systems
(parenterals; ICE inhibitors for treatment and prevention of **seizures**)
IT Drug delivery systems
(tablets; ICE inhibitors for treatment and prevention of **seizures**)
IT 122191-40-6, Interleukin-converting enzyme 186322-81-6, Caspase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICE inhibitors for treatment and prevention of **seizures**)
IT 57-33-0 57-41-0, Phenytoin 77-41-8, Methsuximide 77-67-8, Ethosuximide 99-66-1 115-38-8, Mephobarbital 125-33-7, Primidone 298-46-4, Carbamazepine 439-14-5, Diazepam 461-72-3, Hydantoin 846-49-1, Lorazepam 1622-61-3, Clonazepam 1744-22-5, Riluzole 15687-27-1, Ibuprofen 23887-31-2, Clorazepate 25451-15-4, Felbamate 60142-96-3, Gabapentin 68506-86-5, Vigabatrin 76584-70-8 **84057-84-1**, Lamotrigine 93390-81-9, Fosphenytoin 97240-79-4, Topiramate 115103-54-3, Tiagabine 148553-50-8, Pregabalin 192755-52-5 192756-07-3 244133-31-1 273404-36-7 273404-37-8 853017-36-4 853017-37-5 853017-38-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(ICE inhibitors for treatment and prevention of **seizures**)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1241184 CAPLUS
DOCUMENT NUMBER: 143:483161
TITLE: Mouth dissolvable and meltable, and water dispersable delivery formulation for **antiepileptics**
INVENTOR(S): Chakravorty, Saibal; Hariharan, V.
PATENT ASSIGNEE(S): Rpg Life Sciences Limited, India
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005109990	A2	20051124	WO 2005-IN101	20050404

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2004-MU419 A 20040406
ED Entered STN: 24 Nov 2005
AB A mouth dissolvable and meltable, and water dispersable delivery system for oral administration consisting of an antiepileptic drug, one or more swelling agents, one or more of fillers, one or more of disintegrating agents, and one or more of binders is disclosed. The swelling agent is powdered cellulose, filler is spray dried mannitol, disintegrating agent is crosslinked polyvinyl pyrrolidone and binder is maltodextrin. This system optionally comprises one or more of other **excipients** selected from the group comprising lubricants, sweeteners and flavoring agent.
IC ICM A61K
CC 63-6 (Pharmaceuticals)
ST mouth dissolvable delivery **antiepileptic** binder filler disintegrating agent
IT Acacia
Anticonvulsants
Binders
Dissolution
Fillers
Mouth
Particle size
(mouth dissolvable tablets containing **antiepileptics** and cellulose and mannitol and disintegrating agents and binders)
IT Drug delivery systems
(oral; mouth dissolvable tablets containing **antiepileptics** and cellulose and mannitol and disintegrating agents and binders)

IT Drug delivery systems
(tablets; mouth dissolvable tablets containing **antiepileptics** and cellulose and mannitol and disintegrating agents and binders)
IT 9003-39-8, Polyvinyl pyrrolidone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crosslinked; mouth dissolvable tablets containing **antiepileptics** and cellulose and mannitol and disintegrating agents and binders)
IT 50-70-4, Sorbitol, biological studies **50-99-7**, Glucose, biological studies 57-48-7, Fructose, biological studies 69-65-8, Mannitol 69-79-4, Maltose 9004-34-6, Cellulose, biological studies 9005-25-8, Corn starch, biological studies 9050-36-6, Maltodextrin 11138-66-2, Xanthan gum 74811-65-7, Croscarmellose sodium **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mouth dissolvable tablets containing **antiepileptics** and cellulose and mannitol and disintegrating agents and binders)

L31 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:761734 CAPLUS
DOCUMENT NUMBER: 143:279127
TITLE: Scopolamine-induced **convulsions** in fasted mice after food intake: effects of glucose intake, antimuscarinic activity and **anticonvulsant** drugs
AUTHOR(S): Enginar, Nurhan; Nurten, Asiye; Yamantuerk Celik, Pinar; Acikmese, Baris
CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turk.
SOURCE: Neuropharmacology (2005), 49(3), 293-299
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Aug 2005
AB The present study was performed to further evaluate the contribution of antimuscarinic activity and hypoglycemia to the development of scopolamine-induced convulsions in fasted mice after food intake. The effects of anticonvulsant drugs on convulsions were also evaluated. Antimuscarinic drugs atropine (3 mg/kg) and biperiden (10 mg/kg) were given i.p. to animals fasted for 48 h. Like scopolamine, both drugs induced convulsions after animals were allowed to eat ad libitum. Another group of animals was given glucose (5%) in drinking water during fasting. These animals, although they had normoglycemic blood levels after fasting, also developed convulsions after treated with scopolamine i.p. (3 mg/kg), atropine (3 mg/kg) or biperiden (10 mg/kg) and allowed to eat ad libitum. Among the drugs studied, only valproate (340 mg/kg), gabapentin (50 mg/kg) and diazepam (2.5 and 5 mg/kg) markedly reduced the incidence of scopolamine-induced convulsions. The present results indicate that antimuscarinic activity, but not hypoglycemia, underlies these convulsions which do not respond to most of the conventional anticonvulsant drugs.
CC 1-11 (Pharmacology)
ST scopolamine **convulsion** food intake glucose antimuscarinic **anticonvulsant** drug
IT **Anticonvulsants**
Convulsion
Feeding
Hypoglycemia
Muscarinic antagonists
(scopolamine-induced **convulsions** in fasted mice after food

intake and effects of glucose intake, antimuscarinic activity and **anticonvulsant** drugs)

IT 114-49-8, Scopolamine hydrobromide
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (scopolamine-induced **convulsions** in fasted mice after food intake and effects of glucose intake, antimuscarinic activity and **anticonvulsant** drugs)

IT 50-06-6, Phenobarbital, biological studies 55-48-1, Atropine sulfate 57-41-0, Phenytoin 99-66-1 298-46-4, Carbamazepine 439-14-5, Diazepam 514-65-8, Biperiden 60142-96-3, Gabapentin **84057-84-1**, Lamotrigine
RL: PAC (Pharmacological activity); BIOL (Biological study) (scopolamine-induced **convulsions** in fasted mice after food intake and effects of glucose intake, antimuscarinic activity and **anticonvulsant** drugs)

IT **50-99-7**, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (transport; scopolamine-induced **convulsions** in fasted mice after food intake and effects of glucose intake, antimuscarinic activity and **anticonvulsant** drugs)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:612064 CAPLUS
DOCUMENT NUMBER: 143:139157
TITLE: Preparation of rigid liposomal cochleate
INVENTOR(S): Krause-Elsmore, Sara L.; Mannino, Raphael J.
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005063213	A1	20050714	WO 2004-US42927	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-531546P P 20031219
US 2004-565120P P 20040423

ED Entered STN: 15 Jul 2005

AB Employing liposomes having a high transition temperature at least partially disposed in a matrix, compns. are provided that can be used to deliver one or more cargo moieties, e.g., a drug, a nutrient, an imaging agent and/or nonsteroidal anti-inflammatory drug. The matrix can be a lipid precipitate and/or a cationic bridge. Methods of making and using these compns. preferably cochleates, are also disclosed. Rigid liposomes were obtained from distearoylphosphatidylserine and dextran.

IC ICM A61K009-127
ICS A61K047-02
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 17
IT Adenoma
Alopecia
Alzheimer's disease
Anesthetics
Animal cell
Animal virus
Anti-inflammatory agents
Antibiotics
Anticonvulsants
Antidepressants
Antihistamines
Antimicrobial agents
Antioxidants
Antipsychotics
Antitumor agents
Antiviral agents
Autoimmune disease
Biliary tract, neoplasm
Blood coagulation disorders
Carcinoma
Cholinergic antagonists
Citrus
Decongestants
Eczema
Esophagus, neoplasm
Eubacteria
Expectorants
Flavoring materials
Fungicides
Ginkgo
Graves' disease
Herb
Hypercholesterolemia
Hyperglycemia
Hypericum
Hypertension
Hyssopus officinalis
Imaging agents
Immune disease
Immunostimulants
Immunosuppressants
Inflammation
Leukemia
Leukemia
Leukotriene antagonists
Lymphoma
Malnutrition
Mammary gland, neoplasm
Melanoma
Multiple sclerosis
Myasthenia gravis
Mycosis
Neuroglia, neoplasm
Nutrients
Obesity
Organelle

Origanum
Ovary, neoplasm
Pain
Pancreas, neoplasm
Parasite
Parkinson's disease
Pepper (spice)
Pigments, nonbiological
Plant cell
Plasmids
Poisons, nonbiological source
Prostate gland, neoplasm
Psoriasis
Salvia
Sarcoma
Schizophrenia
Skin, disease
Spices
Stomach, neoplasm
Sweetening agents
Tea products
Testis, neoplasm
Tranquilizers
Uterus, neoplasm
Vanilla
Vasoconstrictors
Vasodilators
(preparation of rigid liposomal cochleate)

IT 50-02-2 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-48-6, Amitriptyline 50-49-7, Imipramine 50-78-2 50-81-7, Vitamin C, biological studies **50-99-7**, Glucose, biological studies 51-61-6, Dopamine, biological studies 52-53-9, Verapamil 53-06-5, Cortisone 53-86-1, Indomethacin 54-11-5 57-41-0 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-92-1, Streptomycin, biological studies 58-22-0 58-82-2, Bradykinin 58-85-5, Biotin 59-01-8, Kanamycin A 59-43-8, Vitamin B1, biological studies 62-49-7, Choline 66-71-7, 1,10-Phenanthroline 67-20-9, Nitrofurantoin 68-19-9, Vitamin B12 69-79-4, Maltose 72-69-5, Nortriptyline 77-41-8, Methsuximide 77-67-8, Ethosuximide 79-09-4, Propionic acid, biological studies 81-07-2, Saccharin 83-88-5, Vitamin B2, biological studies 86-34-0, Phensuximide 86-35-1, Ethotoin 87-89-8, Inositol 89-57-6, Mesalamine 98-92-0, Vitamin B3 103-90-2 110-91-8D, **Morpholine**, derivs. 112-38-9, Undecylenic acid 113-15-5 113-53-1, Dothiepin 117-39-5, Quercetin 124-07-2, Caprylic acid, biological studies 125-33-7, Primidone 126-07-8, Griseofulvin 127-40-2, Lutein 127-48-0, Trimethadione 128-46-1, Dihydrostreptomycin 130-26-7, Clioquinol 144-68-3 148-82-3 298-46-4, Carbamazepine 302-79-4, Vitamin A acid 303-49-1, Clomipramine 379-68-0 439-14-5, Diazepam 446-72-0, Genistein 458-37-7 501-36-0, Resveratrol 512-64-1, Echinomycin 536-59-4, Perillyl alcohol 618-39-3, Benzamidine 645-05-6, Hexamethylmelamine 777-11-7, Haloprogin 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamycin 1404-04-2, Neomycin 1404-55-3, Ristocetin 1404-90-6, Vancomycin 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1421-14-3, Propanidid 1668-19-5, Doxepin 1695-77-8, Spectinomycin 2022-85-7, Flucytosine 2078-54-8, Propofol 2398-96-1, Tolnaftate 2644-64-6 2809-21-4 2954-45-2, Dimyristoylphosphatidylserine 3036-82-6 3947-65-7 4478-93-7, Sulforaphane 4537-77-3 4539-70-2 4696-76-8, Kanamycin B 5681-36-7 7235-40-7, β-Carotene 7261-97-4, Dantrolene 7439-89-6, Iron,

biological studies 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies 7440-09-7, Potassium, biological studies 7440-22-4, Silver, biological studies 7440-39-3, Barium, biological studies 7440-42-8, Boron, biological studies 7440-47-3, Chromium, biological studies 7440-50-8, Copper, biological studies 7440-62-2, Vanadium, biological studies 7440-66-6, Zinc, biological studies 7440-70-2, Calcium, biological studies 7488-56-4, Selenium sulfide 7542-37-2, Paromomycin 7681-93-8 7782-49-2, Selenium, biological studies 8059-24-3, Vitamin B6 8067-82-1, Alphadione 9002-60-2, Corticotropin, biological studies 9004-10-8, Insulin, biological studies 9005-25-8, Starch, biological studies 9007-12-9, Calcitonin 9034-40-6, LHRH 9041-90-1, Angiotensin I 9050-36-6, Maltodextrin 9076-44-2, Chymostatin 10417-94-4, Eicosapentaenoic acid 11000-17-2, Vasopressin 11056-06-7, Bleomycin 11103-57-4, Vitamin A 11128-99-7, Angiotensin II 12001-76-2, Vitamin B 12001-79-5, Vitamin K 12687-51-3, Angiotensin III 13292-46-1, Rifampin 14268-17-8 15307-86-5, Diclofenac 15687-27-1 19698-29-4 19794-93-5, Trazodone 20255-95-2 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1 22832-87-7 22839-47-0, Aspartame 22888-70-6, Silibinin 22916-47-8, Miconazole 23047-25-8, Lofepramine 23593-75-1, Clotrimazole 24305-27-9, Thyroid releasing hormone 25316-40-9, Adriamycin 25451-15-4, Felbamate 25546-65-0, Ribostamycin 27220-47-9, Econazole 27774-13-6, Vanadyl sulfate 28721-07-5, Oxcarbazepine 29767-20-2, Teniposide 30562-34-6, Geldanamycin 32986-56-4, Tobramycin 33069-62-4, Taxol 33507-63-0, Substance P 36322-90-4, Piroxicam 36357-77-4, Phosphoramidon 37321-09-8, Apramycin 37332-99-3, Avoparcin 37517-28-5, Amikacin 37691-11-5, Antipain 39319-82-9, Actinoidin 39324-30-6, Pepstatin 41621-49-2, Ciclopirox olamine 42924-53-8, Nabumetone 51050-59-0, 3,4-Dichloroisocoumarin 51110-01-1, Somatostatin 51798-45-9, Elastatinal 53123-88-9, Rapamycin 54651-05-7, Echinocandin B 54910-89-3, Fluoxetine 55123-66-5, Leupeptin 56391-56-1, Netilmicin 58391-28-9, Leucokinin 58814-86-1, Aculeacin A 58970-76-6, Bestatin 59277-89-3 59729-33-8, Citalopram 60617-12-1, β-Endorphin 61036-62-2, Teicoplanin 61318-90-9 61869-08-7, Paroxetine 64211-45-6, Oxiconazole 64519-82-0, Isomalt 64872-76-0, Butoconazole 65277-42-1, Ketoconazole 65472-88-0, Naftifine 67655-94-1, Amastatin 67915-31-5, Terconazole 68291-97-4, Zonisamide 70288-86-7, Ivermectin 71125-38-7, Meloxicam 71620-89-8 74913-18-1, Dynorphin 78628-80-5, Terbinafine hydrochloride 79217-60-0, Cyclosporin 79404-91-4, Cilofungin 79617-96-2, Sertraline **84057-84-1**, Lamotrigine 84625-61-6, Itraconazole 85650-52-8, Mirtazapine 86386-73-4, Fluconazole 92216-05-2, Distearoylphosphatidylserine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 97240-79-4, Topiramate 101828-21-1, Butenafine 102767-28-2, Levetiracetam 105462-24-6 110588-57-3, Saperconazole 114977-28-5, Taxotere 127779-20-8, Saquinavir 137234-62-9, Voriconazole 150378-17-9, Indinavir 155213-67-5, Ritonavir 159445-62-2, Orientiparcin 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 166663-25-8, Anidulafungin 235114-32-6, Micafungin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of rigid liposomal cochleate)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:493490 CAPLUS
DOCUMENT NUMBER: 143:32332
TITLE: Water dispersible tablet
INVENTOR(S): Gupta, Vinod Kumar; Vaya, Navin; Sougata, Pramanick

PATENT ASSIGNEE(S): Torrent Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051350	A2	20050609	WO 2004-IN312	20041007
WO 2005051350	A3	20050818		
WO 2005051350	B1	20050929		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MU1128 A 20031028
ED Entered STN: 10 Jun 2005
AB This invention relates to a water-dispersible formulation of an active pharmaceutical ingredient or pharmaceutically acceptable salt hereof and one or more adjuvants without the use of swellable clay. More particularly, the invention comprises a dispersible formulation of anti-epileptic drug - lamotrigine. This invention further relates to a process for the preparation of said formulation.
IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
IT Drug delivery systems
(**carriers**; water-dispersible lamotrigine tablet)
IT **Anticonvulsants**
Binders
Dispersion (of materials)
Dyes
Flavoring materials
Particle size distribution
Sieving
(water-dispersible lamotrigine tablet)
IT **84057-84-1**, Lamotrigine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(water-dispersible lamotrigine tablet)

L31 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:325504 CAPLUS
DOCUMENT NUMBER: 142:379390
TITLE: Pharmaceutical formulations comprising microparticles with improved dispersibility, suspendability or wettability
INVENTOR(S): Chickering, Donald E.; Reese, Shaina; Narasimhan, Sridhar; Straub, Julie A.; Bernstein, Howard; Altreuter, David; Huang, Eric K.; Brito, Luis A.; Jain, Rajeev A.

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 324,550.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005079138	A1	20050414	US 2004-955261	20040930
US 2004121003	A1	20040624	US 2002-324558	20021219
PRIORITY APPLN. INFO.:			US 2002-324558	A2 20021219

ED Entered STN: 15 Apr 2005
AB Methods are provided for making a dry powder blend pharmaceutical formulation, comprising the steps of: (a) providing microparticles which comprise a pharmaceutical agent; (b) blending the microparticles with at least one **excipient** in the form of **particles** to form a powder blend; and (c) jet milling the powder blend to form a dry powder blend pharmaceutical formulation having improved dispersibility, suspendability, or wettability as compared to the microparticles of step (a) or the powder blend of step (b). The method can further include dispersing the dry powder blend pharmaceutical formulation in a liquid pharmaceutically acceptable vehicle to make an formulation suitable for injection. Alternatively, the method can further include processing the dry powder blend pharmaceutical formulation into a solid oral dosage form. In one embodiment, the microparticles of step (a) are formed by a solvent precipitation or crystallization process. PLGA microspheres containing mannitol and Tween 80 having number average **particle** size of 1.96 μm, and volume average **particle** size of 4.04 μm were prepared The jet milling provided significant **particle** deagglomeration.
IC ICM A61L009-04
ICS A61K009-14
INCL 424046000; 424489000; 241018000
CC 63-6 (Pharmaceuticals)
IT Antiasthmatics
Antibacterial agents
Anticonvulsants
Antihistamines
Antimicrobial agents
Antipsychotics
Antitumor agents
Antiviral agents
Anxiety
Anxiolytics
Asthma
Bronchodilators
Calcium channel blockers
Epilepsy
Fungicides
Hypnotics and Sedatives
Immunosuppressants
Immunosuppression
Mycosis
Neoplasm
Particle size distribution
Sleep
(methods for making pharmaceutical formulations comprising

microparticles with improved dispersibility, suspendability or wettability)

IT 50-28-2, Estradiol, biological studies 55-98-1, Busulfan 57-41-0, Phenytoin 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 76-25-5, Triamcinolone acetonide 89-57-6, Mesalamine 298-46-4, Carbamazepine 439-14-5, Diazepam 599-79-1, Sulfasalazine 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 846-49-1, Lorazepam 1951-25-3, Amiodarone 2078-54-8, Propofol 3385-03-3, Flunisolide 5534-09-8, Beclomethasone dipropionate 5786-21-0, Clozapine 8064-90-2, Bactrim 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 10118-90-8, Minocycline 18559-94-9, Albuterol 26787-78-0, Amoxicillin 28721-07-5, Oxcarbazepine 28981-97-7, Alprazolam 33069-62-4, Paclitaxel 34346-01-5, Lactic acid glycolic acid copolymer 41340-25-4, Etodolac 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 51110-01-1, Somatostatin 51322-75-9, Tizanidine 51333-22-3, Budesonide 52352-27-9, Poly(hydroxybutyric acid) 53123-88-9, Sirolimus 53714-56-0, Leuprolide 59277-89-3, Acyclovir 59865-13-3, Cyclosporine 68475-42-3, Anagrelide 68693-11-8, Modafinil 70524-20-8 71125-38-7, Meloxicam 72558-82-8, Ceftazidime 73573-87-2, Formoterol 79794-75-5, Loratidine 80474-14-2, Fluticasone propionate 81103-11-9, Biaxin 82410-32-0, Ganciclovir 83799-24-0, Fexofenadine **84057-84-1**, Lamotrigine 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86639-52-3, SN 38 89365-50-4, Salmeterol 92665-29-7, Cefprozil 95058-81-4, Gemcitabine 102190-94-3, Poly(hydroxyvaleric acid) 103370-86-1, Parathyroid hormone-related peptide 104227-87-4, Famciclovir 104987-11-3, Tacrolimus 105102-22-5, Mometasone 107753-78-6, Zafirlukast 111406-87-2, Zileuton 114977-28-5, Docetaxel 115103-54-3, Tiagabine 132539-06-1, Olanzapine 137234-62-9, Voriconazole 137862-53-4, Valsartan 143011-72-7, Granulocyte colony-stimulating factor 146939-27-7, Ziprasidone 155213-67-5, Ritonavir 159989-65-8, Nelfinavir mesylate 162011-90-7, Rofecoxib 169590-42-5, Celecoxib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods for making pharmaceutical formulations comprising microparticles with improved dispersibility, suspendability or wettability)

L31 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:216629 CAPLUS
DOCUMENT NUMBER: 142:285200
TITLE: Nanoparticles for drug delivery
INVENTOR(S): Turos, Edward; Shim, Jeung-Yeop
PATENT ASSIGNEE(S): University of South Florida, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020933	A2	20050310	WO 2004-US28995	20040902
WO 2005020933	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-499904P P 20030902
US 2003-500750P P 20030904
US 2004-568746P P 20040506

ED Entered STN: 11 Mar 2005

AB This invention relates to a unique process for the preparation of polymeric nanoparticles with target mols. bonded to the surface of the **particles** and having sizes of up to 1000 nm, preferably 1-400 nm, more preferably 1-200 nm, that are dispersed homogeneously in aqueous solution To accomplish the above objective, the polymeric nanoparticles of the subject invention are prepared using a novel technique of microemulsion polymerization The resulting aqueous solution of polymeric nanoparticles is comprised of about 1-100 parts per weight of water or buffer, about 1-80 parts per weight of polymeric nanoparticles, which the bioactive mols. are conjugated, about 0.001-10 parts per weight of emulsifier, and about 0.00001-5 parts per weight of radical initiator based on the weight of the solution In the method of this invention, the target drug/target substance is covalently bonded to the polymeric nanoparticles to secure them from outer intervention in vivo or cell culture in vitro until they are exposed at the target site within the cell. Nanoparticles of ethylacrylate-N-methylthiolated 3-lactam copolymer were prepared by a radical polymerization using potassium persulfate as the initiator and the sodium salt of dodecyl sulfate as the surfactant. The **particle** size was 40-80 nm. The antibacterial activity of the nanoparticles is shown.

IC ICM A61K

CC 63-6 (Pharmaceuticals)

IT Analgesics
Anesthetics
Anthelmintics
Anti-inflammatory agents
Antiarrhythmics
Antiasthmatics
Antibacterial agents
Antibiotics
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antihypertensives
Antioxidants
Antipsychotics
Antipyretics
Antithyroid agents
Antitumor agents
Antitussives
Antiviral agents
Anxiolytics
Bacterium (genus)
Blood products
Bronchodilators
Buffers
Chemotherapy

Diuretics
Dopamine agonists
Drug delivery systems
Emulsifying agents
Eukaryota
Expectorants
Fungicides
Hemostatics
Hypnotics and Sedatives
Immunostimulants
Immunosuppressants
Muscarinic antagonists
Muscle relaxants
Prokaryota
Surfactants
(nanoparticles for drug delivery)

IT 50-28-2, Estradiol, biological studies 54-31-9, Furosemide 57-41-0, Phenytoin 58-32-2, Dipyridamole 59-30-3, Folic acid, biological studies 61-33-6, Penicillin G, biological studies 61-68-7, Mefenamic acid 69-89-6D, Xanthine, derivs. 77-26-9, Butalbital 83-43-2, Methylprednisolone 87-33-2, Isosorbide dinitrate 99-66-1, Valproic acid 124-94-7, Triamcinolone 298-46-4, Carbamazepine 439-14-5, Diazepam 446-86-6, Azathioprine 520-85-4, Medroxyprogesterone 846-49-1, Lorazepam 990-73-8, Fentanyl citrate 1406-05-9, Penicillin 1622-61-3, Clonazepam 1951-25-3, Amiodarone 3385-03-3, Flunisolide 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 5786-21-0, Clozapine 10238-21-8, Glyburide 11041-12-6, Cholestyramine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 20830-75-5, Digoxin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 27848-84-6, Nicergoline 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 29122-68-7, Atenolol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34368-04-2, Dobutamine 36322-90-4, Piroxicam 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 50679-08-8, Terfenadine 51333-22-3, Budesonide 52485-79-7, Buprenorphine 53179-11-6, Loperamide 54739-18-3, Fluvoxamine 58581-89-8, Azelastine 59467-70-8, Midazolam 63527-52-6, Cefotaxime 65277-42-1, ,Ketoconazole 68844-77-9, Astemizole 70458-96-7, Norfloxacin 72509-76-3, Felodipine 73590-58-6, Omeprazole 74191-85-8, Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76584-70-8 76824-35-6, Famotidine 79217-60-0, Cyclosporin 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81098-60-4, ,Cisapride 81103-11-9, Clarithromycin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine **84057-84-1**, Lamotrigine 84625-61-6, Itraconazole 85441-61-8, Quinapril 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 87333-19-5, Ramipril 88150-42-9, Amlodipine 91161-71-6, Terbinafine 98319-26-7, Finasteride 103577-45-3, Lansoprazole 105102-22-5, Mometasone 106266-06-2, Risperidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanoparticles for drug delivery)

L31 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1047608 CAPLUS
DOCUMENT NUMBER: 142:254377
TITLE: Valproate decreases inositol biosynthesis
AUTHOR(S): Shaltiel, Galit; Shamir, Alon; Shapiro, Joseph; Ding, Daobin; Dalton, Emma; Bialer, Meir; Harwood, Adrian J.; Belmaker, Robert H.; Greenberg, Miriam L.; Agam,

Galila
CORPORATE SOURCE: Stanley Research Center and Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beersheva, Israel
SOURCE: Biological Psychiatry (2004), 56(11), 868-874
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Dec 2004
AB Lithium and valproate (VPA) are used for treating bipolar disorder. The mechanism of mood stabilization has not been elucidated, but the role of inositol has gained substantial support. Lithium inhibition of inositol monophosphatase, an enzyme required for inositol recycling and de novo synthesis, suggested the hypothesis that lithium depletes brain inositol and attenuates phosphoinositide signaling. Valproate also depletes inositol in yeast, Dictyostelium, and rat neurons. This raised the possibility that the effect is the result of myo-inositol-1-phosphate (MIP) synthase inhibition. Inositol was measured by gas chromatog. Human prefrontal cortex MIP synthase activity was assayed in crude homogenate. INO1 was assessed by Northern blotting. Growth cones **morphol.** was evaluated in cultured rat neurons. We found a 20% in vivo reduction of inositol in mouse frontal cortex after acute VPA administration. As hypothesized, inositol reduction resulted from decreased MIP synthase activity: .21-.28 mmol/LVPA reduced the activity by 50%. Among psychotropic drugs, the effect is specific to VPA. Accordingly, only VPA upregulates the yeast INO1 gene coding for MIP synthase. The VPA derivative N-methyl-2,2,3,3,-tetramethyl-cyclopropane carboxamide reduces MIP synthase activity and has an affect similar to that of VPA on rat neurons, whereas another VPA derivative, valpromide, poorly affects the activity and has no effect on neurons. The rate-limiting step of inositol biosynthesis, catalyzed by MIP synthase, is inhibited by VPA; inositol depletion is a first event shown to be common to lithium and VPA.
CC 1-11 (Pharmacology)
IT **Anticonvulsants**
(**anticonvulsant** mood stabilizers carbamazepine, phenytoin, lamotrigine did not show significant human brain myo-inositol-1-phosphate synthase activity)
IT **84057-84-1**, Lamotrigine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lamotrigine did not show significant human brain myo-inositol-1-phosphate synthase activity)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:999687 CAPLUS
DOCUMENT NUMBER: 141:416046
TITLE: Analeptic and drug combinations
INVENTOR(S): Hughes, Rodney J.; Vaught, Jeffry L.
PATENT ASSIGNEE(S): Cephalon Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004229943	A1	20041118	US 2004-845836	20040514
AU 2004241110	A1	20041202	AU 2004-241110	20040517
CA 2524870	AA	20041202	CA 2004-2524870	20040517
WO 2004103359	A1	20041202	WO 2004-US15408	20040517
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1635807	A1	20060322	EP 2004-752424	20040517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1791397	A	20060621	CN 2004-80013407	20040517
NO 2005005173	A	20051212	NO 2005-5173	20051103
PRIORITY APPLN. INFO.:			US 2003-471302P	P 20030516
			US 2004-845836	A 20040514
			WO 2004-US15408	W 20040517

ED Entered STN: 19 Nov 2004

AB Compns. and methods for the treatment of disorders through the administration of modafinil with M-drugs (modafinil adjunct drugs) are disclosed.

IC ICM A61K031-343
ICS A61K031-165

INCL 514469000; 514617000; 514649000; 514220000; 514259310; 514221000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 15

IT **Anticonvulsants**
Antidepressants
Antipsychotics
Antitumor agents
Cardiovascular agents
Dopamine agonists
Human
Nervous system stimulants
(analeptic and drug combinations containing modafinil)

IT Drug delivery systems
(**carriers**; analeptic and drug combinations containing modafinil)

IT 52-53-9, Verapamil 57-22-7, Vincristine 57-41-0, Phenytoin 298-46-4, Carbamazepine 357-70-0, Galantamine 5786-21-0, Clozapine 15663-27-1, Cisplatin 19216-56-9, Prazosin 20830-75-5, Digoxin 21829-25-4, Nifedipine 25614-03-3, Bromocriptine 33069-62-4, Taxol 36894-69-6, Labetalol 42399-41-7, Diltiazem 60142-96-3, Gabapentin 62571-86-2, Captopril 66104-22-1, Pergolide 68693-11-8, Modafinil 68693-11-8D, Modafinil, salts 75847-73-3, Enalapril **84057-84-1**, Lamotrigine 91374-21-9, Ropinirole 97240-79-4, Topiramate 104632-26-0, Pramipexole 106266-06-2, Risperidone 112111-43-0 114798-26-4, Losartan 114977-28-5, Docetaxel 115103-54-3, Tiagabine 120014-06-4, Donepezil 132539-06-1, Olanzapine 145155-23-3 145258-61-3, Interferon β1 (human fibroblast protein moiety)
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(analeptic and drug combinations containing modafinil)

L31 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902155 CAPLUS
DOCUMENT NUMBER: 141:384286
TITLE: Novel encochleation methods, cochleates and methods of use
INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan; Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA; University of Medicine and Dentistry of New Jersey
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	C1	20050127		
WO 2004091578	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005013854	A1	20050120	US 2004-822230	20040409
EP 1624858	A2	20060215	EP 2004-759375	20040409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:

US 2003-461483P	P	20030409
US 2003-463076P	P	20030415
US 2003-499247P	P	20030828
US 2003-502557P	P	20030911
US 2003-532755P	P	20031224
US 2004-537252P	P	20040115
US 2004-556192P	P	20040324
WO 2004-US11026	W	20040409

ED Entered STN: 28 Oct 2004
AB The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate compns. that include introducing a cargo moiety to a liposome in the presence of a solvent. Also disclosed are cochleates and cochleate compns. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate compns. of the invention, including methods of administration, are also disclosed.
IC ICM A61K009-127
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 17, 18
IT Drug delivery systems
(**carriers**; novel encochleation methods and cochleates and

methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

IT Adenoma
Aggregation
Alopecia
Alzheimer's disease
Analgesics
Anesthetics
Animal virus
Anti-Alzheimer's agents
Anti-infective agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antibiotics
Anticholesteremic agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antihypertensives
Antihypotensives
Antimicrobial agents
Antiobesity agents
Antioxidants
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Antitumor agents
Antiviral agents
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Biliary tract, neoplasm
Blood coagulation disorders
Carcinoma
Carcinoma
Cations
Chelating agents
Cholinergic antagonists
Cognition enhancers
Cystic fibrosis
Cytoprotective agents
Cytotoxic agents
Dairy products
Decongestants
Detergents
Eczema
Esophagus, neoplasm
Expectorants
Flavoring materials
Fungicides
Gene therapy
Genetic vectors
Ginkgo
Gout
Graves' disease
Gums and Mucilages

Headache
Hemophilia
Hemostatics
Hypercholesterolemia
Hyperglycemia
Hypericum
Hypertension
Hypolipemic agents
Hypotension
Imaging agents
Immune disease
Immunostimulants
Immunosuppressants
Infection
Inflammation
Leukemia
Leukotriene antagonists
Lung, neoplasm
Lymphoma
Malnutrition
Mammary gland, neoplasm
Melanoma
Milk
Mouthwashes
Multiple sclerosis
Muscular dystrophy
Myasthenia gravis
Mycosis
Neoplasm
Neuroglia, neoplasm
Nutrients
Obesity
Organelle
Osteoarthritis
Ovary, neoplasm
Packaging materials
Pain
Pancreas, neoplasm
Parasiticides
Parkinson's disease
Pigments, biological
Plasmids
Prostate gland, neoplasm
Psoriasis
Psychotropics
Rheumatoid arthritis
Sarcoma
Schizophrenia
Skin, disease
Stomach, neoplasm
Sweetening agents
Testis, neoplasm
Tranquilizers
Transplant rejection
Uterus, neoplasm
Vaccines
Vasoconstrictors
Vasodilators
(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation

inhibitors)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies
50-12-4, Mephenytoin 50-23-7, Hydrocortisone 50-24-8, Prednisolone
50-48-6, Amitriptyline 50-49-7, Imipramine 51-61-6, Dopamine,
biological studies 52-53-9, Verapamil 53-06-5, Cortisone 53-86-1,
Indomethacin 54-11-5, Nicotine 57-41-0, Phenytoin 57-92-1,
Streptomycin, biological studies 58-22-0, Testosterone 58-82-2,
Bradykinin 59-01-8, Kanamycin A 66-71-7, 1,10-Phenanthroline
67-20-9, Nitrofurantoin 72-69-5, Nortriptyline 77-41-8, Methsuximide
77-67-8, Ethosuximide 79-09-4, Propionic acid, biological studies
86-34-0, Phensuximide 86-35-1, Ethotoin 89-57-6, Mesalamine
103-90-2, Acetaminophen 110-91-8D, **Morpholine**, derivs.
112-38-9, Undecylenic acid 113-15-5D, Ergotamine, derivs. 113-53-1,
Dothiepin 124-07-2, Caprylic acid, biological studies 125-33-7,
Primidone 126-07-8, Griseofulvin 127-48-0, Trimethadione 128-46-1,
Dihydrostreptomycin 130-26-7, Clioquinol 148-82-3, Melphalan
298-46-4, Carbamazepine 302-79-4, Vitamin A acid 303-49-1,
Clomipramine 379-68-0, 18-Hydroxydeoxycorticosterone 439-14-5,
Diazepam 458-37-7, Curcumin 512-64-1, Echinomycin 618-39-3,
Benzamidine 645-05-6, Hexamethylmelamine 777-11-7, Haloprogin
1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamycin
1404-04-2, Neomycin 1404-55-3, Ristocetin 1404-90-6, Vancomycin
1421-14-3, Propanidid 1668-19-5, Doxepin 1695-77-8, Spectinomycin
2022-85-7, Flucytosine 2078-54-8, Propofol 2398-96-1, Tolnaftate
2809-21-4 3947-65-7, Neamine 4696-76-8, Kanamycin B 7261-97-4,
Dantrolene 7488-56-4, Selenium sulfide 7542-37-2, Paromomycin
7681-93-8, Natamycin 8067-82-1, Alphadione 9002-60-2, ACTH, biological
studies 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin
9034-40-6, LH-RH 9041-90-1, Angiotensin I 9076-44-2, Chymostatin
11000-17-2, Vasopressin 11056-06-7, Bleomycin 11128-99-7, Angiotensin
II 12687-51-3, Angiotensin III 13292-46-1, Rifampin 14074-80-7, Zinc
tetraphenyl porphyrin 15307-86-5, Diclofenac 15687-27-1, Ibuprofen
19794-93-5, Trazodone 21829-25-4, Nifedipine 22071-15-4, Ketoprofen
22204-53-1, Naproxen 22832-87-7, Miconazole nitrate 22916-47-8,
Miconazole 23047-25-8, Lofepramine 23593-75-1, Clotrimazole
24305-27-9, Thyroid releasing hormone 25316-40-9, Adriamycin
25451-15-4, Felbamate 25546-65-0, Ribostamycin 27220-47-9, Econazole
28721-07-5, Oxcarbazepine 29767-20-2, Teniposide 30562-34-6,
Geldanamycin 32986-56-4, Tobramycin 33069-62-4, Taxol 33507-63-0,
Substance P (peptide) 36322-90-4, Piroxicam 36357-77-4, Phosphoramidon
37321-09-8, Apramycin 37332-99-3, Avoparcin 37517-28-5, Amikacin
37691-11-5, Antipain 39319-82-9, Actinoidin 39324-30-6, Pepstatin
41621-49-2, Ciclopirox olamine 42924-53-8, Nabumetone 51050-59-0,
3,4-Dichloroisocoumarin 51110-01-1, Somatostatin 51798-45-9,
Elastatinal 53123-88-9, Rapamycin 54651-05-7, Echinocandin B 54910-8
9-3, Fluoxetine 55123-66-5, Leupeptin 56391-56-1, Netilmicin
58391-28-9, Leucokinin 58814-86-1, Aculeacin A 58970-76-6, Bestatin
59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporin
60617-12-1, β-Endorphin 61036-62-2, Teicoplanin 61318-90-9,
Sulconazole 61869-08-7, Paroxetine 64211-45-6, Oxiconazole
64872-76-0, Butoconazole 65277-42-1, Ketoconazole 65472-88-0,
Naftifine 67655-94-1, Amastatin 67915-31-5, Terconazole 68291-97-4,
Zonisamide 70288-86-7, Ivermectin 71125-38-7, Meloxicam 71620-89-8,
Reboxetine 74913-18-1, Dynorphin 78628-80-5, Terbinafine hydrochloride
79404-91-4, Cilofungin 79617-96-2, Sertraline 80619-41-6, Echinocandin
84057-84-1, Lamotrigine 84625-61-6, Itraconazole 85650-52-8,
Mirtazapine 86386-73-4, Fluconazole 93390-81-9, Fosphenytoin
93413-69-5, Venlafaxine 97240-79-4, Topiramate 101828-21-1, Butenafine
102767-28-2, Levetiracetam 105462-24-6 110588-57-3, Saperconazole
114977-28-5, Taxotere 118850-71-8 118850-72-9 118850-73-0

127779-20-8, Saquinavir 135882-23-4, Pneumocandin A4 137234-62-9, Voriconazole 150378-17-9, Indinavir 155213-67-5, Ritonavir 159445-62-2, Orientiparcin 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 166663-25-8, Anidulafungin 235114-32-6, Micafungin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

IT **50-99-7**, Glucose, biological studies 57-50-1, Sucrose, biological studies 69-79-4, Maltose 81-07-2, Saccharine 9050-36-6, Maltodextrin 22839-47-0, Aspartame 64519-82-0, Isomalt
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(sweetening agent; novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

L31 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:778053 CAPLUS
DOCUMENT NUMBER: 142:107203
TITLE: The effect of Vigabatrin, Lamotrigine and Gabapentin on the fertility, weights, sex hormones and biochemical profiles of male rats
AUTHOR(S): Daoud, A. S.; Bataineh, H.; Otoom, S.; Abdul-Zahra, E.
CORPORATE SOURCE: Departments of Neuroscience, College of Medicine, Jordan University of Science and Technology, Irbid, Jordan
SOURCE: Neuroendocrinology Letters (2004), 25(3), 178-183
CODEN: NLETDU; ISSN: 0172-780X
PUBLISHER: Society of Integrated Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Sep 2004
AB PURPOSE: A case control study was conducted to assess the effect of Sabril (Vigabatrin), Lamictal (Lamotrigine) and Neurontin (Gabapentin) on fertility in male rats. Their effect on the body and organs weight and certain biochem. profiles including total serum protein, cholesterol, triglycerides, serum glutamic oxaloacetic transaminase (SCOT), serum glutamic pyruvic transaminase (SGPT), serum testosterone, and FSH levels were also measured. METHODS: several parameters, concerning fertility were measured in 40 albino male rats of Sprague Dawley strain, they were divided into 4 groups, group one received vehicle (distilled water), group two received Vigabatrin in a dose of 200 mg/kg body weight, group three received Lamotrigine in a dose of 30 mg/kg body weight, and group four received Gabapentin 100 mg/kg body weight All the male rats in these groups received the different medications for a complete reproductive cycle (60 days). After 24 h of the last dose, the animals were weighed and autopsied under light ether anesthesia. Parameter of fertility that has been measured in this study includes: sperm count and motility, weight of different reproductive organs, germ cell and interstitial cell population, serum testosterone and FSH levels and assessment of pregnancies in females mixed with tested males. Biochem. profiles such as serum cholesterol, serum triglycerides, serum bilirubin, SCOT, SGPT level are all measured. The results of the histol., histometrical studies and biochem. profiles were compared to that of the control group, and the significance of these results was measured using student's "t" test. RESULTS,: There was significant reduction in the body weight and the weight of the testes, epididymis,
seminal vesicles, ventral prostate, and vas deferens in the antiepileptic

fed male rats in comparison to the control group ($p>0.001$). There was significant reduction in testicular cells population dynamics including both germinal cell types and interstitial cell types in the antiepileptic fed male rats in comparison to the control group. There was also significant reduction in histometrical parameters and sperm dynamics in the antiepileptic fed male rats histologies in comparison to the control group. There was significant reduction in both testosterone and FSH levels ($p<0.001$) in the antiepileptics fed male rats in comparison to the control group. There was also significant reduction in pregnancy rate observed in female rats exposed to the tested male rats among antiepileptic fed male rats compared to controls. The results of biochem. profiles assessment showed significant reduction in serum glucose, serum cholesterol, serum triglycerides levels and significant increase in serum bilirubin, SCOT, and SGPT levels in antiepileptics fed male rats in comparison to the control group. CONCLUSIONS: Fertility rate and other parameters concerned with fertility, sex hormones and certain biochem. profiles were significantly disturbed in male rats fed with three of the second-generation antiepileptic drugs Vigabatrin, Lamotrigine, and Gabapentin, indicating a possible toxic effect of these three medications on sexual organs, liver, and lipid metabolism

CC 1-11 (Pharmacology)

ST vigabatrin lamotrigine gabapentin **antiepileptic** fertility body wt sex hormone

IT **Anticonvulsants**
(AEDs vigabatrin, lamotrigine, gabapentin decreased organ, body weight, fertility rate, fertility parameters, sex hormones, certain biochem. profiles, suggesting possible toxicity on sexual organs, liver, lipid metabolism in male rat)

IT **84057-84-1**, Lamictal
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AED lamotrigine significantly decreased organ, body weight, fertility rate and other fertility parameters, sex hormones, certain biochem. profiles, suggesting possible toxic effect on sexual organs, liver, lipid metabolism in male rat)

IT **50-99-7**, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; vigabatrin, lamotrigine, gabapentin treatment showed significant reduction in serum glucose levels in male rat)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:971868 CAPLUS
DOCUMENT NUMBER: 140:19871
TITLE: Delayed release drug delivery systems containing polymers and method for preparation by mixing and compacting
INVENTOR(S): Hanshermann, Franke; Lennartz, Peter; Raimer, Joern
PATENT ASSIGNEE(S): Desitin Arzneimittel Gmbh, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2003101428 A1 20031211 WO 2003-EP5115 20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10224170 A1 20031211 DE 2002-10224170 20020531
CA 2485080 AA 20031211 CA 2003-2485080 20030515
AU 2003236658 A1 20031219 AU 2003-236658 20030515
BR 2003011512 A 20050222 BR 2003-11512 20030515
EP 1509205 A1 20050302 EP 2003-735396 20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005528428 T2 20050922 JP 2004-508786 20030515
NO 2004005386 A 20041209 NO 2004-5386 20041209
US 2005202088 A1 20050915 US 2005-516268 20050527
PRIORITY APPLN. INFO.: DE 2002-10224170 A 20020531
WO 2003-EP5115 W 20030515

ED Entered STN: 14 Dec 2003

AB The invention relates to a pharmaceutical composition, which has a delayed active substance release and can be obtained by means of a special compacting method for which organic solvents and water are not required. Said pharmaceutical composition preferably exists in the form of individual active substance compartments or breaks down into compartments of this type when brought into contact with aqueous media. Various types of drugs can be formulated with acrylic copolymers. Thus 30 kg of oxcarbazepine and 9 kg of Eudragit RSPO were mixed in a quick mixer (Diosna P 100); the mixture was compacted using a a Gerteis 3 W-Polygran roller compactor applying 15-40 kN/cm at 80°C. The product was disintegrated by forced sieving and classified through a mash. The **particles** were encapsulated in hard gel capsules.

IC ICM A61K009-14

CC 63-6 (Pharmaceuticals)

IT Analgesics
Antiarrhythmics
Anticonvulsants
Antidepressants
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Cholinergic antagonists
Cognition enhancers
Compaction
Dopamine antagonists
Hypnotics and Sedatives
Mixing
Pressure
Temperature
Tranquilizers
(delayed release drug delivery systems containing polymers and method for preparation by mixing and compacting)

IT 61-56-3, Sultiam 79-10-7D, Acrylic acid, esters, polymers 99-66-1, Valproic acid 298-46-4, Carbamazepin **84057-84-1**, Lamotrigine 102767-28-2, Levetiracetam

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delayed release drug delivery systems containing polymers and method for preparation by mixing and compacting)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

Application

ACCESSION NUMBER: 2003:875073 CAPLUS
DOCUMENT NUMBER: 139:354488
TITLE: Pharmaceutical composition containing lamotrigine **particles** of defined **morphology**
INVENTOR(S): Aronhime, Judith; Samburski, Guy
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090693	A2	20031106	WO 2003-US13002	20030423
WO 2003090693	A3	20040108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483103	AA	20031106	CA 2003-2483103	20030423
AU 2003234240	A1	20031110	AU 2003-234240	20030423
EP 1496864	A2	20050119	EP 2003-728552	20030423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005238724	A1	20051027	US 2004-511987	20041021

PRIORITY APPLN. INFO.: US 2002-374923P P 20020423
WO 2003-US13002 W 20030423

ED Entered STN: 07 Nov 2003

AB The present invention provides a pharmaceutical composition comprising a plurality of lamotrigine **particles** having a sp. **surface area** of from about two to about three and a half meters per g. Pharmaceutical compns. falling within the **surface area** criteria for the lamotrigine **particles** include those having a **particle** diameter equal to or less than about 100 μm, preferably about 50 μm, and most preferably 10 μm. The pharmaceutical composition can be formulated into a wide variety of dosage forms for treatment of seizures.

IC ICM A61K
CC 63-6 (Pharmaceuticals)
ST lamotrigine **particle morphol seizure** treatment
IT Phenols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,6-dialkyl; pharmaceutical composition containing lamotrigine

particles of defined **morphol.** and **excipients**
)
IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT Drug delivery systems
(liqs., oral; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)
IT Drug delivery systems
(**particles**; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)
IT Acacia
Anticonvulsants
Chondrules
Egg yolk
Human
Seizures
(pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT Alcohols, biological studies
Bentonite, biological studies
Carbohydrates, biological studies
Caseins, biological studies
Gelatins, biological studies
Kaolin, biological studies
Polyoxyalkylenes, biological studies
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT Drug delivery systems
(solids, oral; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, hydrogenated; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT 9003-01-4D, crosslinked
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Carbomer; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)
IT 9003-39-8D, crosslinked
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Crospovidone; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)

IT 99-96-7D, alkyl esters
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Parabens; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)

IT 7631-86-9, Colloidal silicon dioxide, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)

IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**
)

IT 50-21-5, Lactic acid, biological studies 50-70-4, Sorbitol, biological studies **50-99-7**, **Dextrose**, biological studies
56-81-5, Glycerin, biological studies 57-15-8, Chlorobutanol 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies
57-55-6, Propylene glycol, biological studies 57-88-5, Cholesterol, biological studies 60-00-4, Ethylenediamine tetraacetic acid, biological studies 60-12-8, Phenethyl alcohol 63-42-3, Lactose 64-17-5, Ethyl alcohol, biological studies 64-19-7, Acetic acid, biological studies
69-65-8, Mannitol 72-17-3, Sodium lactate 77-92-9, Citric acid, biological studies 79-41-4D, Methacrylic acid, polymers 81-07-2, Saccharin 87-69-4, biological studies 100-51-6, Benzyl alcohol, biological studies 108-32-7, Propylene carbonate 121-54-0, Benzethonium chloride 127-09-3, Sodium acetate 128-37-0, Butylated hydroxy toluene, biological studies 128-44-9, Sodium saccharin
471-34-1, Calcium carbonate, biological studies 526-95-4, Gluconic acid
527-07-1, Sodium gluconate 532-32-1, Sodium benzoate 546-93-0, Magnesium carbonate 994-36-5, Sodium citrate 1309-48-4, Magnesium oxide, biological studies 1327-43-1, Magnesium aluminum silicate
7447-40-7, Potassium chloride, biological studies 7631-90-5, Sodium bisulfite 7647-14-5, Sodium chloride, biological studies 7681-57-4, Sodium metabisulfite 7758-87-4, Tribasic calcium phosphate 7778-18-9, Calcium sulfate 7789-77-7, Dibasic calcium phosphate dihydrate
8013-17-0, Invert sugar 8027-56-3, Liquid glucose 9000-30-0, Guar gum
9000-65-1, Tragacanth 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol
9003-39-8, Povidone 9004-32-4, Carboxymethylcellulose sodium
9004-53-9, Dextrin 9004-57-3, Ethyl cellulose 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-37-2, Propylene glycol alginate 9005-38-3, Sodium alginate 9050-04-8 9050-36-6, Maltodextrin 9063-38-1, Sodium starch glycolate 11138-66-2, Xanthan gum 14807-96-6, Talc, biological studies 22839-47-0, Aspartame
25013-16-5, Butylated hydroxyanisole 25322-68-3, Polyethylene glycol
36653-82-4, Cetyl alcohol 39404-33-6, Dextrates 54182-62-6D, Polacrilin, potassium form 74811-65-7, Croscarmellose sodium
84057-84-1, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing lamotrigine **particles** of defined **morphol.** and **excipients**)

L31 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757508 CAPLUS
DOCUMENT NUMBER: 139:255389
TITLE: Norepinephrine- and serotonin-reuptake inhibitors for treating visceral pain syndromes
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003077897	A1	20030925	WO 2003-US8155		20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2479350	AA	20030925	CA 2003-2479350		20030317
AU 2003225837	A1	20030929	AU 2003-225837		20030317
US 2003203055	A1	20031030	US 2003-391110		20030317
EP 1485078	A1	20041215	EP 2003-744697		20030317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005526079	T2	20050902	JP 2003-575950		20030317
NO 2004004345	A	20041203	NO 2004-4345		20041013
PRIORITY APPLN. INFO.:			US 2002-364531P	P	20020315
			WO 2003-US8155	W	20030317

OTHER SOURCE(S): MARPAT 139:255389
ED Entered STN: 26 Sep 2003
AB The invention provides a method for treating a visceral pain syndrome in a mammal. The method includes administering an effective amount of a selective norepinephrine (NE)-serotonin (5-HT) reuptake inhibitor (NSRI), e.g., milnacipran.
IC ICM A61K031-165
ICS A61K031-00; A61P025-00
CC 1-11 (Pharmacology)
IT 5-HT reuptake inhibitors
Analgesics
Anti-inflammatory agents
Anti-ischemic agents
Anticonvulsants
Antidepressants
Antidiarrheals
Antiulcer agents
Appetite depressants
Calcium channel blockers
Cholinergic antagonists
Diarrhea
Drug delivery systems
Gastrointestinal agents
Hypnotics and Sedatives
Ischemia
Laxatives
Nervous system stimulants
(norepinephrine-serotonin reuptake inhibitors for treating visceral pain syndromes, and use with other agents)
IT **50-99-7**, D-Glucose, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glucose-electrolyte solution; norepinephrine-serotonin reuptake inhibitors for treating visceral pain syndromes, and use with other agents)

IT 50-06-6, Phenobarbital, biological studies 51-55-8, , Atropine, biological studies 55-63-0, Nitroglycerin 57-27-2, Morphine, biological studies 57-41-0, Phenytoin 59-66-5, Acetazolamide 59-92-7, biological studies 63-42-3, , Lactose 67-52-7D, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. 69-72-7D, Salicylic acid, salicylates, biological studies 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-67-8, Ethosuximide 79-09-4, Propionic acid, biological studies 91-20-3D, Naphthalene, naphthylalkanones 91-40-7D, Fenamic acid, fenamates 99-66-1 101-31-5, Hyoscyamine 120-72-9D, Indole, derivs. 123-30-8D, p-Aminophenol, derivs. 125-33-7, ,Primidone 137-58-6, Lidocaine 288-13-1D, Pyrazole, derivs. 298-46-4, Carbamazepine 300-62-9, Amphetamine 439-14-5, Valium 1622-61-3, , Clonazepam 8029-99-0, Paregoric 8063-16-9, , Psyllium 12794-10-4, Benzodiazepine 19794-93-5, Trazodone 27203-92-5, Tramadol 43200-80-2, Zopiclone 51322-75-9, Tizanidine 53179-11-6, Loperamide 60142-96-3, ,Gabapentin 68693-11-8, Modafinil 82626-48-0, Zolpidem 83150-76-9, , Octreotide **84057-84-1**, Lamotrigine 89565-68-4, Tropisetron 92623-85-3, Milnacipran 93390-81-9, Fosphenytoin 97240-79-4, Topiramate 104632-26-0, ,Pramipexole 106650-56-0, Sibutramine 122852-42-0, , Alosetron 145158-71-0, Tegaserod 148553-50-8, Pregabalin 216382-88-6, Imidazopyridine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(norepinephrine-serotonin reuptake inhibitors for treating visceral pain syndromes, and use with other agents)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:584855 CAPLUS
DOCUMENT NUMBER: 140:104464
TITLE: Pharmacokinetic drug interactions in children taking oxcarbazepine
AUTHOR(S): Sallas, William M.; Milosavljev, Slavica; D'Souza, Joseph; Hossain, Mohammad
CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2003), 74(2), 138-149
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Jul 2003
AB Our objective was to evaluate the drug-drug interactions of oxcarbazepine with coadministered antiepileptic drugs in children. In a clin. trial, pediatric patients receiving an oxcarbazepine dose titrated to 30 to 46 mg · kg-1 · d-1 given twice daily had 1 to 4 blood samples collected per patient for population pharmacokinetic anal. of oxcarbazepine's major bioactive 10-monohydroxy metabolite. With the use of NONMEM, 7 concomitant antiepileptic drugs and 12 addnl. covariates were examined for their effects on the pharmacokinetics of 10-monohydroxy metabolite. In addition, for each concomitant antiepileptic drug, the ratio of its mean concentration with coadministration of oxcarbazepine to that without

coadministration at baseline was calculated to evaluate the effect of oxcarbazepine on the coadministered antiepileptic drugs. The population pharmacokinetic data for 10-monohydroxy metabolite consisted of a total of 376 observations from 109 patients, aged 3 to 17 yr. Body **surface area** and 3 antiepileptic drugs (carbamazepine, phenobarbital, and phenytoin) were significant predictors of the apparent clearance of 10-monohydroxy metabolite, whereas height was a significant predictor of apparent volume Weight-normalized clearance of 10-monohydroxy metabolite was higher in young children than in older children and adults. Carbamazepine, phenobarbital, or phenytoin administered with oxcarbazepine increased the apparent clearance of 10-monohydroxy metabolite by 31% to 35%, whereas carbamazepine levels decreased by 15% and phenobarbital levels increased by 14%. Oxcarbazepine has a low propensity to inhibit or induce oxidative enzymes. Young children could be given higher milligrams-per-kilogram oxcarbazepine doses than older children and adults to achieve the same mean steady-state concentration of 10-monohydroxy metabolite.

The adjustment is based simply on body size.

CC 1-4 (Pharmacology)

ST oxcarbazepine **antiepileptic** pharmacokinetic interaction **seizure** child body size

IT **Anticonvulsants**
Human
Seizures
(pharmacokinetic drug interactions in children taking oxcarbazepine)

IT 50-06-6, Phenobarbital, biological studies 57-41-0, Phenytoin 99-66-1 298-46-4, Carbamazepine 28721-07-5, Oxcarbazepine 60142-96-3, Gabapentin **84057-84-1**, Lamotrigine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic drug interactions in children taking oxcarbazepine)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:319348 CAPLUS
DOCUMENT NUMBER: 138:331688
TITLE: Methods of suppressing microglial activation and systemic inflammatory responses
INVENTOR(S): Laskowitz, Daniel T.; Matthew, William D.; McMillian, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 957,909.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003077641	A1	20030424	US 2002-252120		20020923
US 2002164789	A1	20021107	US 2001-957909		20010921
PRIORITY APPLN. INFO.:			US 1998-77551P	P	19980311
			US 1999-260430	B2	19990301
			US 2001-957909	A2	20010921

ED Entered STN: 25 Apr 2003

AB Methods of suppressing the activation of microglial cells in the Central Nervous System (CNS), methods of ameliorating or treating the neurol.

effects of cerebral ischemia or cerebral inflammation, and methods of combating specific diseases that affect the CNS by administering a compound that binds to microglial receptors and prevents or reduces microglial activation are described. ApoE receptor binding peptides that may be used in the methods of the invention are also described, as are methods of using such peptides to treat peripheral inflammatory conditions such as sepsis. Also described are methods of screening compds. for the ability to suppress or reduce microglial activation. Injection of ApoE (133-149) in mice suppressed serum levels of TNFα and IL-6 following LPS administration.

IC ICM A61K038-17
ICS A61K038-10; C12Q001-68; A61K038-00; C12N007-00; C12N007-01; C12N005-00; C12N005-02; A61K039-12
INCL 435006000; 514013000; 435235100; 435325000; 424186100
CC 1-7 (Pharmacology)
IT Anti-Alzheimer's agents
Anticonvulsants
Antioxidants
Antiparkinsonian agents
Brain, disease
Central nervous system
Dopamine antagonists
Drug delivery systems
Drug screening
Glutamate antagonists
Human
Mammalia
(ApoE receptor binding peptides suppressing microglial activation and systemic inflammatory responses)
IT Drug delivery systems
(**carriers**, across blood-brain barrier, conjugates; ApoE receptor binding peptides suppressing microglial activation and systemic inflammatory responses)
IT Alzheimer's disease
Atherosclerosis
Encephalitis
Epilepsy
Multiple sclerosis
Parkinson's disease
Schizophrenia
Sepsis
(treatment of; ApoE receptor binding peptides suppressing microglial activation and systemic inflammatory responses)
IT 57-41-0, Phenytoin 77-67-8, Ethosuximide 99-66-1, Valproic acid 298-46-4, Carbamazepine 4368-28-9, Tetrodotoxin 25451-15-4, Felbamate 60142-96-3, Gabapentin **84057-84-1**, Lamotrigine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**anticonvulsant**; ApoE receptor binding peptides suppressing microglial activation and systemic inflammatory responses)

L31 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:154224 CAPLUS
DOCUMENT NUMBER: 138:193294
TITLE: Expandable gastric retention device containing pharmaceutical compositions
INVENTOR(S): Ayres, James W.
PATENT ASSIGNEE(S): The State of Oregon Acting by and Through the State Board of Higher Education On Behalf of Oregon State University, USA

SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015745	A1	20030227	WO 2001-US46146	20011022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2456976	AA	20030227	CA 2001-2456976	20011022
EP 1416914	A1	20040512	EP 2001-995328	20011022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017123	A	20040928	BR 2001-17123	20011022
CN 1543337	A	20041103	CN 2001-823544	20011022
JP 2005501097	T2	20050113	JP 2003-520705	20011022
NO 2004000611	A	20040416	NO 2004-611	20040211
US 2004219186	A1	20041104	US 2004-778917	20040213
ZA 2004002066	A	20050509	ZA 2004-2066	20040315
PRIORITY APPLN. INFO.:			US 2001-313078P P	20010816
			WO 2001-US46146 W	20011022

ED Entered STN: 28 Feb 2003

AB The present application concerns gastric retention devices formed from compns. comprising polymeric materials, such as polysaccharides, and optional addnl. materials including **excipients**, therapeutics, and diagnostics, that reside in the stomach for a controlled and prolonged period of time. Dry powders of xanthan gum and locust bean gum were mixed intimately were converted to dried films. The dried films were compressed with the help of specially made punches and dies. A series of dies with decreasingly narrow internal diams. were used. A punch pushes the film from one die into the next die, followed by pushing of the film by another punch into the next die. This process takes place in succession until a point is reached where the film is small enough to put into a desired capsule size.

IC ICM A61K009-00
ICS A61K009-20; A61K047-36

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Adrenoceptor agonists
Adrenoceptor antagonists
Analgesics
Anesthetics
Antacids
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-infective agents
Antiarrhythmics
Antibiotics
Anticonvulsants
Antidepressants

Antidiabetic agents
Antidotes
Antiemetics
Antihistamines
Antihypertensives
Antimicrobial agents
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Antitumor agents
Appetite depressants
Appetite stimulants
Cardiovascular agents
Cholinergic agonists
Cholinergic antagonists
Contraceptives
Cystic fibrosis
Deodorants (personal)
Dietary supplements
Digestive tract
Dissolution
Diuretics
Dizziness
Dopamine agonists
Drug bioavailability
Fungicides
Gastric juice
Human
Hypnotics and Sedatives
Imaging agents
Immunomodulators
Immunosuppressants
Intestinal juice
Ion exchangers
Medical goods
Muscle relaxants
Nervous system stimulants
Plasticizers
Psychotropics
Stomach
Urinary system
Vagina
Vasodilators
Wilson's disease
(expandable gastric retention device containing pharmaceutical compns.)

IT 50-44-2, Mercaptopurine 50-53-3, Chlorpromazine, biological studies 51-63-8, Dextroamphetamine sulfate 52-01-7, Spironolactone 54-31-9, Furosemide 58-14-0, Pyrimethamine 58-38-8, Prochlorperazine 59-66-5, Acetazolamide 63-89-8, Colfosceril palmitate 71-27-2, Succinylcholine chloride 89-57-6, Mesalazine 148-82-3, Melphalan 154-42-7, Thioguanine 305-03-3, Chlorambucil 315-30-0, Allopurinol 396-01-0, Triamterene 440-17-5, Trifluoperazine hydrochloride 554-13-2, Lithium carbonate 637-32-1, Proguanil hydrochloride 813-93-4, Bismuth citrate 1508-76-5, Procyclidine hydrochloride 2152-44-5, Betamethasone valerate 5534-09-8, Beclomethasone dipropionate 8064-90-2, Co-trimoxazole 9000-40-2, Locust bean gum 9004-65-3, HPMC 11138-66-2, Xanthan gum 12650-69-0, Mupirocin 13492-01-8, Tranylcypromine sulfate 18559-94-9, Albuterol 20830-75-5, Digoxin 25122-46-7, Clobetasol propionate

25953-19-9, Cefazolin 26787-78-0, Amoxicillin 29457-07-6, Ticarcillin disodium 30516-87-1, Zidovudine 31677-93-7, Bupropion hydrochloride 35121-78-9, Epoprostenol 42924-53-8, Nabumetone 51481-61-9, Cimetidine 54965-21-8, Albendazole 55268-75-2, Cefuroxime 59277-89-3, Acyclovir 61177-45-5, Clavulanate potassium 61336-70-7, Amoxicillin trihydrate 64211-46-7, Oxiconazole nitrate 64228-81-5, Atracurium besylate 66357-35-5, Ranitidine 66357-59-3, Ranitidine hydrochloride 70059-30-2, Cimetidine hydrochloride 71486-22-1, Vinorelbine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73590-58-6, Omeprazole 76095-16-4, Enalapril maleate 78246-49-8, Paroxetine hydrochloride 79902-63-9, Simvastatin 80474-14-2, Fluticasone propionate **84057-84-1**, Lamotrigine 89365-50-4, Salmeterol 91374-20-8, Ropinirole hydrochloride 94749-08-3, Salmeterol xinafoate 95233-18-4, Atovaquone 96946-42-8, Cisatracurium besylate 99614-01-4, Ondansetron hydrochloride 103628-46-2, Sumatriptan 119413-54-6, Topotecan hydrochloride 121679-13-8, Naratriptan 124750-99-8, Losartan potassium 124832-27-5, Valacyclovir hydrochloride 134678-17-4, Lamivudine 139110-80-8, Zanamivir 142373-60-2, Tirofiban hydrochloride 155141-29-0, Rosiglitazone maleate 161814-49-9, Amprenavir 161973-10-0, Esomeprazole magnesium 162011-90-7, Rofecoxib 179463-17-3, Caspofungin acetate 188062-50-2, Abacavir sulfate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expandable gastric retention device containing pharmaceutical compns.)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133030 CAPLUS
DOCUMENT NUMBER: 138:163577
TITLE: Improving neurological functions
INVENTOR(S): Chez, Michael G.
PATENT ASSIGNEE(S): Carn-Aware LLC, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003013514	A1	20030220	WO 2002-US22341		20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2006052428	A1	20060309	US 2005-486077		20050210
PRIORITY APPLN. INFO.:			US 2001-310710P	P	20010808
			US 2001-325136P	P	20010927
			WO 2002-US22341	W	20020715

OTHER SOURCE(S): MARPAT 138:163577
ED Entered STN: 21 Feb 2003
AB The present invention relates to materials and methods for treating neurol. diseases and disorders including but not limited to epilepsy and

autism, as well as general cognitive problems. Preferred compds. include carnosine and homocarnosine and N-acetyl, methylated (anserine, ophidine), decarboxylated (carcinine) and tauryl derivs. of carnosine and homocarnosine.

IC ICM A61K031-415
ICS A61P025-00

CC 1-11 (Pharmacology)

IT Alzheimer's disease
Anti-Alzheimer's agents
Anticonvulsants
Antidepressants
Cognition enhancers
Cognitive disorders
Down's syndrome
Drug delivery systems
Drug interactions
Epilepsy
Human
Nervous system, disease
Nervous system agents
Psychostimulants
(agents for improving neurol. functions such as carnosine derivs. and combination with other agents)

IT Drug delivery systems
(**carriers**; agents for improving neurol. functions such as carnosine derivs. and combination with other agents)

IT Drug delivery systems
(**excipients**; agents for improving neurol. functions such as carnosine derivs. and combination with other agents)

IT 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin 56-12-2, GABA, biological studies 57-41-0, Phenytoin 59-66-5, Acetazolamide 77-67-8, Ethosuximide 86-35-1, Ethotoin 99-66-1, Valproic Acid 115-38-8, Mephobarbital 125-33-7, Primidone 127-48-0, Trimethadione 298-46-4, Carbamazepine 439-14-5, Diazepam 846-49-1, Lorazepam 1622-61-3, Clonazepam 23887-31-2, Clorazepate 25451-15-4, Felbamate 28721-07-5, Oxcarbazepine 60142-96-3, Gabapentin 68506-86-5, Vigabatrin **84057-84-1**, Lamotrigine 97240-79-4, Topiramate 102767-28-2, Levetiracetam 115103-54-3, Tiagabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**anticonvulsant**; agents for improving neurol. functions such as carnosine derivs. and combination with other agents)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:28550 CAPLUS
DOCUMENT NUMBER: 139:17479
TITLE: Neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation
AUTHOR(S): Rekling, Jens C.
CORPORATE SOURCE: Department 828, Biological Research, H. Lundbeck A/S, Valby, DK-2500, Den.
SOURCE: Neuroscience Letters (2003), 335(3), 167-170
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Jan 2003

AB Some anticonvulsants show neuroprotective effects, and may be of use in reducing neuronal death resulting from stroke or traumatic brain injury. Here I report that a broad range of anticonvulsants protect cells in hippocampal slice cultures from death induced by oxygen/glucose deprivation (OGD). Hippocampal slice cultures were submitted to 1 h OGD and the resulting cell death was quantified 24 h later using a novel automated fluorescent scanning method. The classical anticonvulsants phenobarbital, phenytoin, ethosuximide, chlordiazepoxide and midazolam all significantly and dose-dependently reduced cell death induced by OGD. The newer anticonvulsants carbamazepine, felbamate, lamotrigine, tiagabine, and oxcarbazepine also had significant neuroprotective effects, but gabapentin, valproic acid (10 mM), levetiracetam and retigabine were not neuroprotective at a concentration up to 300 μM. In conclusion, several classical and newer anticonvulsants have neuroprotective properties in an in vitro model that simulates cerebral ischemia.

CC 1-11 (Pharmacology)
Section cross-reference(s): 14

ST neuroprotectant **anticonvulsant** hippocampus oxygen glucose

IT Ischemia
(cerebral; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Nerve, disease
(death; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Brain
(hippocampus; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Brain, disease
(ischemia; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Cell death
(neuron; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Anti-ischemic agents
Anticonvulsants
Disease models
(neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Cytoprotective agents
(neuroprotective; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT Brain, disease
(trauma; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT 7782-44-7, Oxygen, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT 50-06-6, Phenobarbital, biological studies 57-41-0, Phenytoin 58-25-3, Chlordiazepoxide 77-67-8, Ethosuximide 99-66-1, Valproic acid 298-46-4, Carbamazepine 25451-15-4, Felbamate 28721-07-5, Oxcarbazepine 59467-70-8, Midazolam 60142-96-3, Gabapentin **84057-84-1**, Lamotrigine 102767-28-2, Levetiracetam 115103-54-3, Tiagabine 150812-12-7, Retigabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)

IT **50-99-7**, D-Glucose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; neuroprotective effects of **anticonvulsants** in rat hippocampal slice cultures exposed to oxygen/glucose deprivation)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:676002 CAPLUS
DOCUMENT NUMBER: 137:222039
TITLE: New crystal forms of lamotrigine and processes for their preparations
INVENTOR(S): Garti, Nissim; Berkovich, Yana; Dolitzky, Ben-Zion; Aronhime, Judith; Singer, Claude; Lieberman, Anita; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068398	A1	20020906	WO 2002-US6160	20020227
WO 2002068398	C2	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439468	AA	20020906	CA 2002-2439468	20020227
US 2003018030	A1	20030123	US 2002-86157	20020227
US 6861426	B2	20050301		
EP 1390355	A2	20040225	EP 2002-706471	20020227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004526714	T2	20040902	JP 2002-567912	20020227
US 2005171107	A1	20050804	US 2005-45355	20050131
PRIORITY APPLN. INFO.:			US 2001-271688P	P 20010227
			US 2002-86157	A1 20020227
			WO 2002-US6160	W 20020227

ED Entered STN: 08 Sep 2002
AB The present invention relates to lamotrigine, a useful agent for anti-epilepsia. New crystal forms of lamotrigine-containing mols. of the solvent in stoichiometric ratios are disclosed. Processes for preparing the new crystal forms of lamotrigine and dosage forms are also provided. For example, 2 g of lamotrigine anhydrous and about 80 mL of ethanol were charged in a three-necked bottomed round flask equipped with a mech. stirrer, a condenser and a thermometer. The suspension was stirred for about 24 h without heating at about 25° and the solid phase was separated by filtration, producing lamotrigine Form H, i.e., lamotrigine ethanol monosolvate.
IC ICM C07D253-075

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 75
ST lamotrigine crystal form prepn hydrate solvate **antiepileptic**
IT **Anticonvulsants**
Crystal **morphology**
Drug delivery systems
Polymorphism (crystal)
(preparation of crystal forms of lamotrigine as **antiepileptic**)
IT 67-66-3, Chloroform, uses 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(precipitation by; preparation of crystal forms of lamotrigine as **antiepileptic**)
IT **375347-20-9**, Lamotrigine hydrate **454695-00-2**
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as **antiepileptic**)
IT 64-17-5, Ethanol, processes 67-56-1, Methanol, processes 67-63-0, Isopropanol, processes 67-64-1, Acetone, processes 68-12-2, Dimethylformamide, processes 108-10-1, Methyl isobutyl ketone 1634-04-4, Methyl tert-butyl ether
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(preparation of crystal forms of lamotrigine as **antiepileptic**)
IT **84057-84-1**, Lamotrigine
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as **antiepileptic**)
IT **454695-02-4 454695-03-5 454695-04-6**
454695-05-7 454695-06-8 454695-07-9
454695-08-0 454695-09-1 454695-10-4
454695-11-5 454695-12-6 454695-13-7
454695-15-9
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(preparation of crystal forms of lamotrigine as **antiepileptic**)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:396644 CAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid **carriers** for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6248363	B1	20010619	US 1999-447690	19991123
CA 2391923	AA	20010531	CA 2000-2391923	20001122
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T2	20030527	JP 2001-539423	20001122
PRIORITY APPLN. INFO.:			US 1999-447690 A	19991123
			WO 2000-US32255 W	20001122

ED Entered STN: 01 Jun 2001

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A composition contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.

IC ICM A61K009-14
ICS A61K009-16; A61K009-20; A61K009-46; A61K009-48; A61K009-50; A61K009-54

CC 63-6 (Pharmaceuticals)

IT Drug delivery systems
(capsules; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Drug delivery systems
(controlled-release; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Glycerides, biological studies
Sterols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Mucopolysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparinoids; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Drug delivery systems
(implants; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Sexual behavior
(impotence; solid **carriers** for improved delivery of active

ingredients in pharmaceutical compns.)
IT Drug delivery systems
(lozenges; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Drug delivery systems
(microspheres; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Drug delivery systems
(nanocapsules; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Drug delivery systems
(oral; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Antioxidants
(pharmaceutical; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Analgesics
Anti-inflammatory agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antihypertensives
Antimalarials
Antipsychotics
Antitumor agents
Anxiolytics
Fungicides
Hypnotics and Sedatives
Immunosuppressants
Muscarinic antagonists
Muscle relaxants
Plasticizers
Protozoacides
Sweetening agents
Tranquilizers
Vaccines
(solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Enkephalins
Fatty acids, biological studies
Growth factors, animal
Interferons
Interleukins
Macrolides
Nucleic acids
Nucleotides, biological studies
Opioids
Peptides, biological studies
Platelet-derived growth factors
Tocopherols
Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Drug delivery systems
(solids; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)
IT Drug delivery systems

(syrups; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Drug delivery systems
(tablets; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Drug delivery systems
(topical; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor necrosis factor receptor:Fc region; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Drug delivery systems
(vaginal; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, hydrogenated, ethoxylated; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT 9001-92-7, Protease 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT 50-14-6, Ergocalciferol 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-34-0, Propantheline bromide 50-56-6, Oxytocin, biological studies 51-15-0, Pralidoxime chloride 51-43-4, Epinephrine 51-48-9, L-Thyroxine, biological studies 51-55-8, Atropine, biological studies 51-60-5, Neostigminemethyl sulfate 52-01-7, Spironolactone 52-24-4, Thiotepa 53-43-0, Dehydroepiandrosterone 55-98-1, Busulphan 57-13-6, Urea, biological studies 57-22-7, Vincristine 57-64-7, Physostigmine salicylate 57-83-0, Progesterone, biological studies 57-94-3, Tubocurarine chloride 59-05-2, Methotrexate 60-31-1, Acetylcholine chloride 62-31-7, Dopamine hydrochloride 63-91-2, L-Phenylalanine, biological studies 65-28-1, Phentolamine mesylate 66-76-2, Dicoumarol 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 68-19-9, Vitamin b12 69-65-8, D-Mannitol 70-51-9, Deferoxamine 71-27-2, Suxamethonium chloride 74-89-5, Methanamine, biological studies 76-57-3, Codeine 76-90-4, Mepenzolate bromide 76-99-3, Methadone 77-19-0, Dicyclomine 87-33-2, Isosorbide dinitrate 89-57-6, Mesalamine 90-82-4, Pseudoephedrine 101-26-8, Pyridostigmine bromide 104-31-4, Benzonatate 113-15-5, Ergotamine 113-92-8, Chlorpheniramine 114-07-8, Erythromycin 114-80-7, Neostigmine bromide 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-40-2, Lutein 129-06-6, Warfarin sodium 131-49-7, Diatrizoate meglumine 140-64-7, Pentamidine isethionate 147-94-4, Cytarabine 154-21-2, Lincomycin 155-97-5, Pyridostigmine 298-46-4, Carbamazepine 298-57-7, Cinnarizine 298-81-7, Methoxsalen 299-42-3, Ephedrine 300-62-9, Amphetamine 302-79-4, Tretinoin 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 303-98-0, Coenzyme Q10 321-64-2, Tacrine 359-83-1, Pentazocine 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 502-65-8, Lycopene 511-12-6, Dihydroergotamine 520-85-4, Medroxyprogesteron 577-11-7, Sodium docusate 595-33-5 596-51-0, Glycopyrrolate 616-91-1, Acetylcysteine 665-66-7, Amantadine hydrochloride 737-31-5, Diatrizoate sodium 865-21-4, Vinblastine 911-45-5, Clomiphene 1115-70-4, Metformin hydrochloride 1134-47-0,

Baclofen 1264-72-8, Colistin sulfate 1319-82-0, Aminocaproic acid 1397-89-3, Amphotericin b 1403-66-3, Gentamycin 1404-90-6, Vancomycin 1405-20-5, Polymyxin B sulfate 1405-37-4, Capreomycin sulfate 1405-87-4, Bacitracin 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1492-18-8, Leucovorin calcium 1501-84-4, Rimantadine hydrochloride 1684-40-8, Tacrine hydrochloride 1695-77-8, Spectinomycin 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 2016-88-8, Amiloride hydrochloride 3056-17-5, Stavudine 3485-62-9, Clidinium bromide 3778-73-2, Isofosfamide 3930-20-9, Sotalol 4291-63-8, Cladribine 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 5534-95-2, Pentagastrin 6493-05-6, Pentoxifylline 7261-97-4, Dantrolene 7414-83-7, Disodium etidronate 7481-89-2, Zalcitabine 7648-98-8, Ambenonium 7689-03-4, Camptothecin 8068-28-8, Colistimethate sodium 9001-27-8, Factor VIII 9001-28-9, Factor IX 9002-01-1, Streptokinase 9002-60-2, Corticotropin, biological studies 9002-61-3, Chorionic gonadotropin 9004-17-5, NPH insulin 9004-99-3, Polyethylene glycol stearate 9005-63-4D, Polyoxyethylene sorbitan, fatty acid esters 9007-92-5, Glucagon, biological studies 9015-68-3, Asparaginase 9034-40-6, Gonadotropin-releasing hormone 9039-53-6, Urokinase 9041-08-1, Dalteparin sodium 9041-93-4, Bleomycin sulfate 9087-70-1, Aprotinin 10238-21-8, Glibenclamide 10540-29-1, Tamoxifen 10596-23-3, Clodronic acid 11000-17-2, Vasopressin 11061-68-0, Insulin (human) 11103-57-4, Vitamin A 12001-79-5, Vitamin K 12584-58-6, Porcine insulin 13265-10-6, Methscopolamine 15307-86-5, Diclofenac 15500-66-0, Pancuronium bromide 15574-96-6, Pizotifen 15663-27-1, Cisplatin 15686-51-8, Clemastine 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 15826-37-6, Cromolyn sodium 16679-58-6, Desmopressin 16960-16-0, Cosyntropin 17230-88-5, Danazol 18323-44-9, Clindamycin 18559-94-9, Albuterol 18883-66-4, Streptozocin 19356-17-3, Calcifediol 20537-88-6, Amifostine 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21215-62-3, Human calcitonin 21256-18-8, Oxaprozin 21679-14-1, Fludarabine 21829-25-4, Nifedipine 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-32-5, Terbutaline sulfate 23214-92-8, Doxorubicin 23288-49-5, Probucol 24356-60-3, Cephapirin sodium 25126-32-3, Sincalide 25322-68-3D, PEG, esters 25523-97-1, Dexchlorpheniramine 25618-55-7D, Polyglycerol, fatty acid esters 25812-30-0, Gemfibrozil 26839-75-8, Timolol 27164-46-1, Cefazolin sodium 27203-92-5, Tramadol 27215-38-9, Glycerol monolaurate 29094-61-9, Glipizide 29122-68-7, Atenolol 29767-20-2, Teniposide 30516-87-1, Zidovudine 32222-06-3, Calcitriol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 33515-09-2, Gonadorelin 33564-30-6, Cefoxitin sodium 34787-01-4, Ticarcillin 34911-55-2, Bupropion 35607-66-0, Cefoxitin 36791-04-5, Ribavirin 38304-91-5, Minoxidil 41340-25-4, Etodolac 41575-94-4, Carboplatin 42057-22-7, Mezlocillin sodium 42540-40-9, Cefamandole nafate 42924-53-8, Nabumetone 43200-80-2, Zopiclone 47931-85-1, Salmon calcitonin 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 50700-72-6, Vecuronium bromide 51110-01-1, Somatostatin 51322-75-9, Tizanidine 51333-22-3, Budesonide 51384-51-1, Metoprolol 51481-61-9, Cimetidine 53123-88-9, Sirolimus 53179-11-6, Loperamide 53230-10-7, Mefloquine 53910-25-1, Pentostatin 54063-53-5, Propafenone 54910-89-3, Fluoxetine 54965-21-8, Albendazole 55142-85-3, Ticlopidine 56180-94-0, Acarbose 57248-88-1, Pamidronate disodium 59277-89-3, Acyclovir 59467-70-8, Midazolam 59703-84-3, Piperacillin sodium 59865-13-3, Cyclosporine 60142-96-3, Neurontin 61270-78-8, Cefonicid sodium 61379-65-5, Rifapentine 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 62893-19-0, Cefoperazone 63585-09-1, Foscarnet sodium 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 64228-81-5, Atracurium besylate 64544-07-6, Cefuroxime axetil 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66376-36-1, Alendronate 68099-86-5, Bepridil hydrochloride 68401-81-0, Ceftizoxime

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

IT 68506-86-5, Vigabatrin 69049-74-7, Nedocromil sodium 69655-05-6, Didanosine 69756-53-2, Halofantrine 70288-86-7, Ivermectin 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71486-22-1, Vinorelbine 72432-03-2, Miglitol 72559-06-9, Rifabutine 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74103-06-3, Ketorolac 74356-00-6, Cefotetan disodium 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 75706-12-6, Leflunomide 76420-72-9, Enalaprilat 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81161-17-3, Esmolol hydrochloride 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 82952-64-5, Trimetrexate glucuronate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony stimulating factor 83881-51-0, Cetirizine 83905-01-5, Azithromycin **84057-84-1**, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 88669-04-9, Trospectomycin 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94749-08-3, Salmeterol xinafoate 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98319-26-7, Finasteride 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 104987-11-3, Tacrolimus 105462-24-6, Risedronic acid 106133-20-4, Tamsulosin 106392-12-5, Oxirane, polymer with methyloxirane, block 106650-56-0, Sibutramine 106819-53-8, Doxacurium chloride 106861-44-3, Mivacurium chloride 107648-80-6, Cefepime hydrochloride 107753-78-6, Zafirlukast 109319-16-6, Factor VIII 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113427-24-0 113665-84-2, Clopidogrel 113852-37-2, Cidofovir 115103-54-3, Tiagabine 116094-23-6, Insulin aspart 117976-89-3, Rabeprazole 118072-93-8, Zoledronate 118292-40-3, Tazarotene 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 124832-26-4, Valaciclovir 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1, Paricalcitol 133040-01-4, Eprosartan 133107-64-9, Insulin lispro 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139110-80-8, Zanamivir 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139639-23-9, Tissue type plasminogen activator 142128-59-4, Terzolin 143003-46-7, Alglucerase 143011-72-7, Granulocyte colony stimulating factor 143831-71-4 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprelvekin 146961-76-4, Alatrofloxacin 147059-72-1, Trovafloxacin 148553-50-8, Pregabalin 151126-32-8, Pramlintide 153559-49-0, Targretin 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 157810-81-6, Indinavir sulfate 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 160337-95-1, Insulin glargine 162011-90-7, Rofecoxib 165101-51-9, Becaplermin 169148-63-4, Insulin detemir 169590-42-5, Celecoxib

171599-83-0, Sildenafil citrate 173146-27-5, Denileukin diftitox
191588-94-0, TNK-tPA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid **carriers** for improved delivery of active ingredients in pharmaceutical compns.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:320910 CAPLUS
DOCUMENT NUMBER: 135:267035
TITLE: Valproate, but not lamotrigine, induces ovarian **morphological** changes in Wistar rats
AUTHOR(S): Roste, Line Sveberg; Tauboll, Erik; Berner, Aasmund; Isojarvi, Jouko It; Gjerstad, Leif
CORPORATE SOURCE: Department of Neurology, Rikshospitalet/The National Hospital, University of Oslo, Oslo, N-0027, Norway
SOURCE: Experimental and Toxicologic Pathology (2001), 52(6), 545-552
CODEN: ETPAEK; ISSN: 0940-2993
PUBLISHER: Urban & Fischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 May 2001
AB Valproate (VPA) medication is associated with development of polycystic ovaries, menstrual disorders and hormonal changes in women with epilepsy. We sought to determine if changes in the ovaries also occurred in an animal model without epilepsy, and whether this effect could be related to a carcinogenic effect expressed by overexpression of p53. A potentially alternative antiepileptic drug, lamotrigine (LTG), was evaluated simultaneously. To this end, female Wistar rats were fed perorally with VPA 400 mg/kg/day (n = 15), VPA 600 mg/kg/day (n = 20), LTG 10 mg/kg/day (n = 15) or control solution (n = 15) for 90-95 days. There was a significant, dose-dependent increase in the number of follicular cysts, reduction in the number of corpora lutea and reduction of ovarian weight in the VPA group. No ovarian pathol. was observed in the LTG group. In neither of the groups were **morphol.** changes seen in other organs, nor was there any overexpression of the tumor suppressor gene p53 found. An alternative antiepileptic drug, LTG, showed no ovarian pathol., and there were no light microscopic changes in other organs, or evidence of pathol. p53 overexpression in the LTG-treated animals.
CC 1-11 (Pharmacology)
ST **anticonvulsant** valproate lamotrigine p53 gene ovary
IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(TP53; valproate, but not lamotrigine, induces ovarian **morphol**. changes in Wistar rats)
IT Ovary, disease
(cyst; valproate, but not lamotrigine, induces ovarian **morphol**. changes in Wistar rats)
IT **Anticonvulsants**
Carcinogens
Menstrual disorder
(valproate, but not lamotrigine, induces ovarian **morphol.** changes in Wistar rats)
IT 99-66-1 **84057-84-1**, Lamotrigine

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(valproate, but not lamotrigine, induces ovarian **morphol.** changes in Wistar rats)
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:493923 CAPLUS
DOCUMENT NUMBER: 127:203891
TITLE: NMDA receptor-mediated pilocarpine-induced **seizures**: characterization in freely moving rats by microdialysis
AUTHOR(S): Smolders, Ilse; Khan, Ghous M.; Manil, Jacqueline; Ebinger, Guy; Michotte, Yvette
CORPORATE SOURCE: Department of Physiology and Physiopathology, Vrije Universiteit Brussel, Brussels, 1090, Belg.
SOURCE: British Journal of Pharmacology (1997), 121(6), 1171-1179
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Aug 1997
AB Pilocarpine administration has been used as an animal model for temporal lobe epilepsy since it produces several **morphol.** and synaptic features in common with human complex partial seizures. Little is known about changes in extracellular neurotransmitter concns. during the seizures provoked by pilocarpine, a non-selective muscarinic agonist. Focally evoked pilocarpine-induced seizures in freely moving rats were provoked by intrahippocampal pilocarpine (10 mM for 40 min at a flow rate of 2 μl min-1) administration via a microdialysis probe. Concomitant changes in extracellular hippocampal glutamate, γ-aminobutyric acid (GABA) and dopamine levels were monitored and simultaneous electrocorticog. was performed. The animal model was characterized by intrahippocampal perfusion with the muscarinic receptor antagonist atropine (20 mM), the sodium channel blocker tetrodotoxin (1 μM) and the N-methyl-D-aspartate (NMDA) receptor antagonist MK-801 (dizocilpine maleate, 100 μM). The effectiveness of locally (600 μM) or systemically (10 mg kg-1 day-1) applied lamotrigine against the pilocarpine-induced convulsions was evaluated. Pilocarpine initially decreased extracellular hippocampal glutamate and GABA levels. During the subsequent pilocarpine-induced limbic convulsions, extracellular glutamate, GABA and dopamine concns. in hippocampus were significantly increased. Atropine blocked all changes in extracellular transmitter levels during and after co-administration of pilocarpine. All pilocarpine-induced increases were completely prevented by simultaneous tetrodotoxin perfusion. Intrahippocampal administration of MK-801 and lamotrigine resulted in an elevation of hippocampal dopamine levels and protected the rats from the pilocarpine-induced seizures. Pilocarpine-induced convulsions developed in the rats which received lamotrigine perorally. Pilocarpine-induced seizures are initiated via muscarinic receptors and further mediated via NMDA receptors. Sustained increases in extracellular glutamate levels after pilocarpine perfusion are related to the limbic seizures. These are arguments in favor of earlier described NMDA receptor-mediated excitotoxicity. Hippocampal dopamine release may be functionally important in epileptogenesis and may participate in the anticonvulsant effects of MK-801 and lamotrigine. The pilocarpine-stimulated hippocampal GABA, glutamate and dopamine levels

reflect neuronal vesicular release.
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
ST NMDA receptor pilocarpine **seizure** neurotransmitter hippocampus; **anticonvulsant** pilocarpine **seizure** neurotransmitter hippocampus
IT **Anticonvulsants**
Convulsion
Disease models
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT Muscarinic receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA-binding; NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT Brain
(hippocampus; NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT 92-13-7, Pilocarpine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT 51-55-8, Atropine, biological studies 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT 77086-22-7, (+)-MK-801 **84057-84-1**, Lamotrigine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and muscarinic receptors)
IT 51-61-6, Dopamine, biological studies 56-12-2, GABA, biological studies 56-86-0, Glutamic acid, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA receptor-mediated pilocarpine-induced **seizures** and characterization in freely moving rats by microdialysis in relation to neurotransmitters of hippocampus and **anticonvulsants** and

muscarinic receptors)
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:440156 CAPLUS
DOCUMENT NUMBER: 119:40156
TITLE: New method for the determination of four **antiepileptic** drugs in human plasma by high performance liquid chromatography
AUTHOR(S): Meyler, M.; Kelly, M. T.; Smyth, M. R.
CORPORATE SOURCE: Sch. Chem. Sci., Dublin City Univ., Dublin, Ire.
SOURCE: Chromatographia (1993), 36, 27-32
CODEN: CHRGB7; ISSN: 0009-5893
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Aug 1993
AB The concurrent administration of several antiepileptic drugs for the treatment of seizure disorders has become common practice. Lamotrigine is a new antiepileptic given in combination with other antiepileptic drugs, but which is not routinely measured in clin. labs. An isocratic high-performance liquid chromatog. method is described for the simultaneous measuring lamotrigine, carbamazepine, phenobarbital and phenytoin within 10 min. The chromatog. system used an Hichrom Spherisorb CN column (20 cm x 4 mm, i.d., 5 μm **particle** size), a μBondapak CN precolumn, and a mobile phase consisting of methanol : acetonitrile : 5 mM sodium acetate (5 : 20 75: by volume, pH adjusted to 6.3 with acetic acid). BWA 725C was used as internal standard The drugs were extracted from 200 μL of plasma with Et acetate, acetonitrile and 5 mM sodium acetate. After evaporation of the organic layer and reconstitution in mobile phase, 25 μL of extract was eluted with mobile phase at a flow rate of 1.2 mL/min. The eluted drugs were detected by their absorption at 205 nm and quantified from their peak heights. The method was found to be rapid, relatively simple to perform and sufficiently sensitive to determine each drug over its entire therapeutic range. Lower limits of detection varied from 50-100 ng/mL, absolute recoveries from 93-98%, and mean intra- and inter-assay CVs were <3.0%.
CC 1-1 (Pharmacology)
ST **antiepileptic** simultaneous detn blood HPLC; liq chromatog
antiepileptic simultaneous detn blood; lamotrigine carbamazepine phenobarbital phenytoin blood HPLC
IT Blood analysis
(simultaneous determination of several **antiepileptics** in human, by isocratic HPLC method)
IT **Anticonvulsants** and **Antiepileptics**
(simultaneous determination of, in human plasma by HPLC)
IT Chromatography, column and liquid
(high-performance, simultaneous determination of several **antiepileptics** in human plasma by isocratic)
IT 50-06-6, Phenobarbital, analysis 57-41-0, Phenytoin 298-46-4, Carbamazepine **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human plasma by HPLC, in concurrent administration of other **antiepileptics**)

L31 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:93715 CAPLUS
DOCUMENT NUMBER: 118:93715
TITLE: A liquid chromatographic assay using a high-speed

column for the determination of lamotrigine, a new **antiepileptic** drug, in human plasma
AUTHOR(S): Fazio, A.; Artesi, C.; Russo, M.; Trio, R.; Oteri, G.; Pisani, F.
CORPORATE SOURCE: 1st Neurol. Clin., Univ. Messina, Messina, Italy
SOURCE: Therapeutic Drug Monitoring (1992), 14(6), 509-12
CODEN: TDMODV; ISSN: 0163-4356
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Mar 1993
AB A sensitive, specific and rapid liquid-chromatog. method for the determination of the new antiepileptic drug lamotrigine (LTG) in human plasma is described. The method involves the use of a com. available 3-μm **particle** size normal-phase column and a microflow-cell-equipped UV detector. Extraction is carried out with Et acetate after alkalinization on a 100-μL plasma sample containing LTG and 3,5-diamino-6-(2-methoxyphenyl)-1,2,4-triazine as internal standard The residue is reconstituted with 50 μL of ethanol, and 5 μL of the final solution is injected into the column. Elution is carried out at 34° using n-hexane/absolute ethanol/35% ammonia (80:20:0.25 by volume) as mobile phase at a flow rate of 2.0 mL/min. Detection is at 313 nm. The chromatog. separation requires <3 min and the sensitivity limit is <0.01 mg/L. Recovery is 88-96.2%, whereas within-day and day-to-day coeffs. of variation are between 4.1 and 7.7%.
CC 1-1 (Pharmacology)
IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human blood by HPLC)

MSP

L38 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:322096 CAPLUS
DOCUMENT NUMBER: 144:369762
TITLE: Preparation of biphenyl derivatives and analogs thereof as canniboid receptor ligands and methods of use
INVENTOR(S): Dolle, Roland E.; Worm, Karin; Zhou, Q. Jean
PATENT ASSIGNEE(S): Adolor Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 81 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006074086	A1	20060406	US 2005-242318	20051003
WO 2006041841	A1	20060420	WO 2005-US35677	20051004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

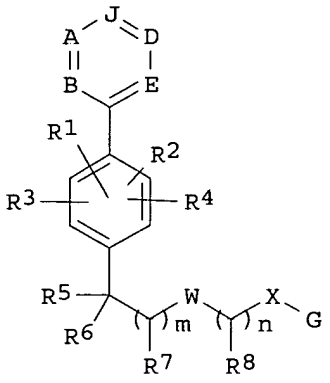
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-616024P P 20041005
US 2005-242318 A 20051003

OTHER SOURCE(S): MARPAT 144:369762

ED Entered STN: 07 Apr 2006

GI



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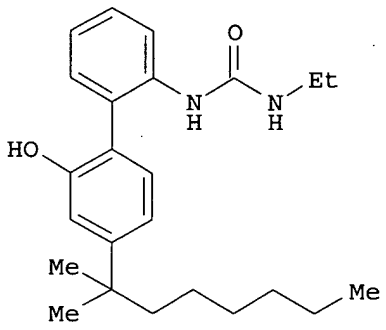


II

AB Title compds. I [R1-4 independently = H, alkyl, alkoxy, etc.; R5 and R6 independently = H, alkyl or taken together with the carbon atom to which they are attached to form a 3-8-membered carbocyclic or heterocyclic ring; each R7 and R8 independently = H, alkyl, halo, etc.; J = N or (un)substituted C, provided that no more than two of A, B, D, E and J are N; A, B, D and E independently = N or (un)substituted C; G = alkyl, acyl, aryl, etc.; W = bond, O, S, CH2, etc.; X = bond, O, -CH=CH-, etc.; m and n independently = 1-5], and their pharmaceutical salts, are prepared and disclosed as canniboid receptor ligands. Thus, e.g., II was prepared by Suzuki coupling of 2-aminophenylboronic acid with resin bound bromophenol derivative (preparation described). Tested compds. were found to bind to human CB1 and/or CB2 receptor with affinity ranging from 0.1-5000 nM. Further, pharmaceutical compns. containing these compds., and methods for their pharmaceutical use are disclosed. In certain embodiments, the compds. are agonists and/or ligands of cannabinoid receptors and may be useful, inter alia, for treating and/or preventing pain, gastrointestinal disorders, genitourinary disorders, inflammation, glaucoma, auto-immune diseases, ischemic conditions, immune-related disorders, and neurodegenerative diseases, for providing cardioprotection against ischemic and reperfusion effects, for inducing apoptosis in malignant cells, and as an appetite stimulant.

INCL 514237500; 544161000

CC 25-2 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63

IT 50-48-6 57-27-2, biological studies 57-41-0 57-42-1 59-92-7, biological studies 76-41-5 76-42-6 76-57-3 76-99-3 77-07-6 125-28-0 125-29-1 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 359-83-1 437-38-7 466-99-9 469-62-5 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 1972-08-3 2323-36-6 13956-29-1 15686-91-6 20594-83-6 27203-92-5, Tramadol 28860-95-9, Carbidopa

42408-82-2 52485-79-7 53179-11-6 53648-55-8 56030-54-7
60142-96-3 71195-58-9 **84057-84-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for use in co-administration; preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

IT 110-78-1 110-91-8, **Morpholine**, reactions 372-09-8, Cyanoacetic acid 1795-48-8, Isopropyl isocyanate 5570-18-3, 2-Aminophenylboronic acid 15159-40-7, N-Chlorocarbonylmorpholine 30418-59-8, 3-Aminophenylboronic acid 30992-29-1 61147-43-1, 3-Benzyloxybenzonitrile 76566-95-5 214360-75-5 380430-66-0 882038-99-5 882039-00-1 882039-01-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

L38 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:673292 CAPLUS
DOCUMENT NUMBER: 143:172866
TITLE: Preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattle J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 427 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068460	A1	20050728	WO 2004-US42720	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006025453	A1	20060202	US 2004-17505	20041220
PRIORITY APPLN. INFO.:			US 2003-531693P P	20031222

OTHER SOURCE(S): MARPAT 143:172866
ED Entered STN: 29 Jul 2005
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are

not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazoledioxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

IC ICM C07D417-12
ICS C07D275-02; C07D417-14; A61K031-427; A61P035-00; A61P029-00

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 50-18-0, Cyclophosphamide 50-48-6, Amitriptyline 51-21-8, 5-Fluorouracil 53-03-2, Prednisone 53-86-1, Indomethacin 57-22-7, Vincristine 59-05-2, Methotrexate 72-69-5, Nortriptyline 298-46-4, Carbamazepine 378-44-9, β-Methasone 446-86-6, Azothioprine 599-79-1, Sulfasalazine 9005-49-6, Heparin, biological studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1, Naproxen 33069-62-4, Paclitaxel 36322-90-4, Piroxicam 60142-96-3, Gabapentin 65271-80-9, Mitoxantrone 75706-12-6, Leflunomide 79217-60-0, Cyclosporin **84057-84-1**, Lamotrigine 85622-93-1, Temozolomide 95058-81-4, Gemcitabine 105857-23-6, Alteplase 143653-53-6, Abciximab 147245-92-9, Glatiramer acetate 148553-50-8, Pregabalin 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 188627-80-7, Eftifibatide 191588-94-0, Tenecteplase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

IT 50-85-1 62-53-3, Phenylamine, reactions 67-36-7 67-47-0 67-64-1, Acetone, reactions 71-43-2, Benzene, reactions 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 77-55-4 78-81-9, Isobutylamine 78-82-0, Isobutyronitrile 78-96-6 79-46-9, 2-Nitropropane 85-38-1, 3-Nitrosalicylic acid 86-51-1, 2,3-Dimethoxybenzaldehyde 88-15-3 89-55-4 89-56-5, 5-Methylsalicylic acid 89-98-5, 2-Chlorobenzaldehyde 92-54-6 93-02-7, 2,5-Dimethoxybenzaldehyde 95-54-5, 1,2-Phenylenediamine, reactions 98-01-1, 2-Furancarboxaldehyde, reactions 98-03-3, 2-Formylthiophene 98-09-9, Phenylsulfonyl chloride 98-80-6, Phenylboronic acid 98-86-2, Acetophenone, reactions 98-88-4, Benzoyl chloride 98-98-6, Picolinic acid 100-10-7 100-46-9, Benzylamine, reactions 100-49-2, Cyclohexylmethanol 100-52-7, Benzaldehyde, reactions 100-58-3, Phenylmagnesium bromide 100-60-7 103-49-1, Dibenzylamine 103-67-3, N-Benzyl-N-methylamine 106-41-2, p-Bromophenol 108-23-6, Isopropyl chloroformate 108-91-8, Cyclohexylamine, reactions 109-61-5, Propyl chloroformate 109-73-9, Butylamine, reactions 109-83-1 109-89-7, Diethylamine, reactions 110-73-6 110-78-1, Propyl isocyanate 110-85-0, Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8, **Morpholine**, reactions 111-42-2, reactions 111-49-9 120-14-9, 3,4-Dimethoxybenzaldehyde 120-21-8, 4-Diethylaminobenzaldehyde 120-43-4 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 121-51-7 121-90-4 121-92-6, 3-Nitrobenzoic acid 122-98-5 123-11-5, 4-Methoxybenzaldehyde, reactions 123-38-6, Propionaldehyde, reactions 123-75-1, Pyrrolidine, reactions 135-00-2 135-02-4, 2-Methoxybenzaldehyde 140-28-3, N,N'-Dibenzylethane-1,2-diamine 142-25-6 149-73-5, Trimethylorthoformate 321-14-2, 5-Chlorosalicylic

acid 344-25-2, D-Proline 349-43-9 406-87-1, 4,4,4-Trifluorobutyraldehyde 420-90-6 434-45-7 446-36-6 446-52-6, 2-Fluorobenzaldehyde 447-61-0, 2-Trifluoromethylbenzaldehyde 454-89-7, 3-Trifluoromethylbenzaldehyde 456-48-4, 3-Fluorobenzaldehyde 459-57-4, 4-Fluorobenzaldehyde 460-40-2 498-60-2, 3-Furaldehyde 498-62-4, 3-Formylthiophene 498-94-2, 4-Piperidinecarboxylic acid 498-95-3, 3-Piperidinecarboxylic acid 503-29-7, Azetidine 527-69-5, 2-Furancarbonyl chloride 529-20-4, 2-Methylbenzaldehyde 534-22-5, 2-Methylfuran 535-75-1, 2-Piperidinecarboxylic acid 554-14-3, 2-Methylthiophene 567-61-3 585-70-6 587-04-2, 3-Chlorobenzaldehyde 591-31-1, 3-Methoxybenzaldehyde 594-19-4, tert-Butyllithium 606-18-8 611-20-1, 2-Cyanophenol 611-24-5 613-69-4, 2-Ethoxybenzaldehyde 616-24-0, 3-Pentanamine 616-34-2, Methyl glycinate 616-44-4, 3-Methylthiophene 618-27-9 619-19-2, 4-Nitrosalicylic acid 620-02-0 621-31-8 624-78-2 625-45-6, Methoxyacetic acid 626-56-2 630-19-3, 2,2-Dimethylpropanal 651-70-7, 2-(Trifluoroacetyl)thiophene 656-42-8 659-28-9, 4-Trifluoromethoxybenzaldehyde 698-63-5, reactions 704-38-1 765-30-0, Cyclopropylamine 920-39-8, Isopropylmagnesium bromide 927-77-5, Propylmagnesium bromide 930-27-8, 3-Methylfuran 931-50-0, Cyclohexylmagnesium bromide 1003-09-4, 2-Bromothiophene 1003-31-2, 2-Thiophenecarbonitrile 1068-55-9, Isopropylmagnesium chloride 1072-67-9, 3-Amino-5-methylisoxazole 1122-60-7 1192-58-1 1204-60-0, [1,1'-Biphenyl]-3-carboxaldehyde 1423-26-3, 3-Trifluoromethylphenylboronic acid 1484-84-0, 2-Piperidineethanol 1692-15-5, 4-Pyridinylboronic acid 1692-25-7, Pyridin-3-ylboronic acid 1700-37-4 1722-12-9, 2-Chloropyrimidine 1730-25-2, Allylmagnesium bromide 1857-20-1 1874-23-3, Methyl 5-nitro-2-furoate 1885-14-9, Phenyl chloroformate 1888-75-1, Isopropyllithium 1899-24-7 2026-48-4 2032-35-1 2039-67-0 2133-40-6 2211-64-5 2402-95-1 2562-38-1 2627-86-3 2689-59-0 2759-28-6, N-Benzylpiperazine 2762-32-5, 2-Piperazinecarboxylic acid 2786-07-4, 2-Thienyllithium 2799-21-5 2987-16-8 3002-94-6, Cyclopropyllithium 3082-64-2 3405-77-4 3433-37-2, 2-Piperidinemethanol 3674-13-3, 2,3-Dibromopropionic acid ethyl ester 3694-52-8, 3-Nitro-1,2-phenylenediamine 3789-59-1 3886-69-9 4138-26-5, 3-Piperidinecarboxamide 4265-16-1, 2-Benzofurancarboxaldehyde 4276-09-9, D-Valinol 4333-56-6, Cyclopropylbromide 4418-61-5, 1H-Tetrazol-5-amine 4606-65-9, 3-Piperidinemethanol 4747-21-1, N-Isopropyl-N-methylamine 5006-62-2 5271-67-0, 2-Thiophenecarbonyl chloride 5333-83-5 5382-16-1, 4-Piperidinol 5473-12-1, Methyl N-methylglycinate 5779-95-3, 3,5-Dimethylbenzaldehyde 5834-16-2 5856-62-2 5856-63-3 5973-71-7, 3,4-Dimethylbenzaldehyde 6165-69-1, 3-Thiopheneboronic acid 6193-47-1 6250-76-6 6287-38-3, 3,4-Dichlorobenzaldehyde 6542-60-5, Cyclopropylacetonitrile 6662-17-5 6859-99-0, 3-Piperidinol 6921-34-2, Benzylmagnesium chloride 6973-60-0, 1-Methyl-2-pyrrolecarboxylic acid 7051-34-5, Cyclopropylmethylbromide 7210-75-5 7311-34-4, 3,5-Dimethoxybenzaldehyde 10200-59-6, 2-Thiazolecarboxaldehyde 10203-08-4, 3,5-Dichlorobenzaldehyde 10242-08-7 10242-10-1 13349-82-1 13515-93-0 13679-70-4 13679-75-9 13734-41-3 13808-64-5 13889-98-0 14305-17-0 14321-27-8, N-Benzyl-N-ethylamine 14610-37-8, N-Methyl-N-tert-butylamine 15231-41-1 15433-83-7 16114-47-9 16466-97-0 17249-80-8, 3-Chlorothiophene 17573-92-1 17766-28-8 19524-06-2, 4-Bromopyridine hydrochloride 20173-04-0 20409-48-7 20980-22-7 20989-17-7 21921-76-6 22078-59-7 22838-58-0 23074-10-4 23356-96-9 29138-64-5 29668-44-8 30084-91-4 32085-88-4, 3,5-Difluorobenzaldehyde 32559-18-5 33208-98-9 33240-34-5, Cyclopentylmagnesium bromide 34035-04-6 34036-07-2, 3,4-Difluorobenzaldehyde 34328-61-5, 3-Chloro-4-fluorobenzaldehyde 34592-47-7 34803-66-2 39515-51-0 39890-42-1 40114-49-6,

N-Benzylpiperid-3-one 40172-95-0 42142-52-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

IT 42142-55-2 45347-82-8, 3-Azetidinol 52130-30-0 52480-43-0
52771-21-8, 3-Trifluoromethoxybenzaldehyde 55745-70-5 55745-96-5
56286-73-8 57260-67-0 57260-71-6 57699-45-3, 4-tert-Butoxybenzaldehyde 62348-13-4, 5-Isoxazolecarbonyl chloride 64951-50-4
65058-23-3 66414-02-6 68820-12-2 68832-13-3 70753-36-5
77873-76-8, 3-**Morpholinecarboxylic** acid 79852-25-8
81097-48-5 81661-26-9 84538-33-0 94098-56-3 94651-33-9,
2-Trifluoromethoxybenzaldehyde 95201-93-7 100243-39-8 103003-01-6,
2-**Morpholinemethanol** 104706-47-0 110013-19-9 119461-40-4
119692-41-0 123221-93-2 123297-88-1, 6-Benzofurancarboxaldehyde
128796-39-4, 4-Trifluoromethylphenylboronic acid 135217-58-2
135427-08-6 147701-78-8 152932-57-5 177971-32-3 180736-67-8
184637-48-7 188816-39-9 189321-66-2 204339-72-0 300582-83-6, 2-**Morpholinecarboxylic** acid 473734-69-9 473734-71-3
473734-74-6 608537-49-1 608537-54-8 608537-74-2 612541-21-6
654683-69-9 654683-71-3 681510-00-9 731006-06-7 779340-46-4
860805-90-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:638859 CAPLUS
DOCUMENT NUMBER: 143:153384
TITLE: Preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Biju, Purakkattle J.; Taveras, Arthur G.; Yu, Younong; Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 593 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

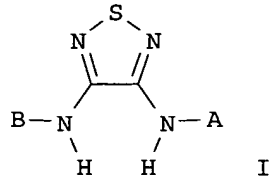
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066147	A1	20050721	WO 2004-US42060	20041216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-531311P P 20031219

US 2003-531713P P 20031222

OTHER SOURCE(S): MARPAT 143:153384
ED Entered STN: 22 Jul 2005
GI



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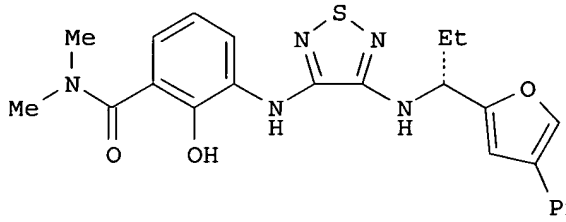

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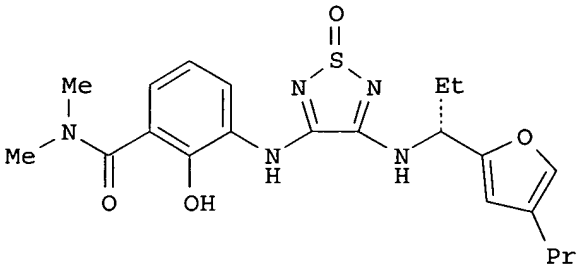


III

AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH2), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

IC ICM C07D285-10
ICS C07D417-12; C07D417-14; A61K031-433; A61K031-4436

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 50-48-6, Amitriptyline 53-86-1, Indomethacin 72-69-5, Nortriptyline 298-46-4, Carbamazepine 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1, Naproxen 36322-90-4, Piroxicam 60142-96-3, Gabapentin **84057-84-1**, Lamotrigine 148553-50-8, Pregabalin 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

IT 50-85-1 62-53-3, Benzenamine, reactions 67-36-7 67-47-0 71-43-2, Benzene, reactions 75-31-0, 2-Propanamine, reactions 75-64-9, reactions 77-55-4 78-81-9 78-82-0 78-96-6 79-44-7 79-46-9 85-38-1 86-51-1 88-15-3 89-55-4 89-56-5 89-98-5 92-54-6 93-02-7 95-54-5, 1,2-Benzenediamine, reactions 98-01-1, 2-Furancarboxaldehyde, reactions 98-03-3, 2-Thiophenecarboxaldehyde 98-09-9, Benzenesulfonyl chloride 98-80-6 98-86-2, reactions 98-88-4, Benzoyl chloride 98-98-6, 2-Pyridinecarboxylic acid 100-10-7 100-46-9, Benzenemethanamine, reactions 100-49-2, Cyclohexanemethanol 100-52-7, Benzaldehyde, reactions 100-58-3 100-60-7 103-49-1 103-67-3 103-71-9, reactions 106-41-2 106-48-9 108-23-6 108-91-8, Cyclohexanamine, reactions 109-01-3 109-61-5 109-83-1 109-89-7, reactions 109-90-0 110-73-6 110-78-1 110-85-0, Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8, **Morpholine**, reactions 111-42-2, reactions 111-49-9 120-14-9 120-21-8 120-43-4 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 120-83-2 121-51-7 121-88-0 121-90-4 121-92-6 122-98-5 123-11-5, reactions 123-38-6, Propanal, reactions 123-75-1, Pyrrolidine, reactions 135-00-2 135-02-4 140-28-3 142-25-6 321-14-2 344-25-2, D-Proline 349-43-9 406-87-1 420-90-6 434-45-7 446-36-6 446-52-6 447-61-0 454-89-7 456-48-4 459-57-4 460-40-2 498-60-2, 3-Furancarboxaldehyde 498-62-4, 3-Thiophenecarboxaldehyde 498-94-2, 4-Piperidinecarboxylic acid 498-95-3, 3-Piperidinecarboxylic acid 503-29-7, Azetidine 527-69-5, 2-Furancarbonyl chloride 529-20-4 534-22-5 535-75-1, 2-Piperidinecarboxylic acid 554-14-3 567-61-3 585-70-6 587-04-2 591-20-8 591-31-1 594-19-4 606-18-8 609-70-1 611-20-1 611-24-5 611-71-2 613-69-4 616-24-0, 3-Pentanamine 616-44-4 620-02-0 621-31-8 624-78-2 625-45-6 626-56-2 630-19-3 651-70-7 656-42-8 659-28-9 698-63-5, reactions 704-38-1 765-30-0, Cyclopropanamine 872-31-1 920-39-8 927-77-5 930-27-8 931-50-0 1003-09-4 1003-31-2, 2-Thiophenecarbonitrile 1072-67-9 1111-92-8 1122-60-7 1192-58-1 1204-60-0, [1,1'-Biphenyl]-3-carboxaldehyde 1423-26-3 1484-84-0, 2-Piperidineethanol 1589-82-8 1692-15-5 1692-25-7 1700-37-4 1722-12-9 1730-25-2 1857-20-1 1874-23-3 1885-14-9 1888-75-1 1899-24-7 2026-48-4 2039-67-0 2133-40-6 2402-95-1 2562-38-1 2627-86-3 2689-59-0 2759-28-6 2762-32-5, 2-Piperazinecarboxylic acid 2786-07-4 2799-21-5 2987-16-8 3002-94-6 3082-64-2 3173-56-6 3405-77-4 3433-37-2, 2-Piperidinemethanol 3674-13-3 3694-52-8 3789-59-1 3886-69-9 4138-26-5, 3-Piperidinecarboxamide 4265-16-1, 2-Benzofurancarboxaldehyde 4276-09-9 4333-56-6 4412-91-3, 3-Furanmethanol 4418-61-5, 1H-Tetrazol-5-amine 4606-65-9, 3-Piperidinemethanol 4747-21-1 4747-71-1 5006-62-2 5271-67-0, 2-Thiophenecarbonyl chloride 5333-83-5 5382-16-1, 4-Piperidinol 5473-12-1 5680-79-5 5779-95-3 5834-16-2 5856-62-2 5856-63-3 5973-71-7 6165-69-1 6193-47-1 6250-76-6 6287-38-3 6542-60-5, Cyclopropaneacetonitrile 6662-17-5 6859-99-0, 3-Piperidinol 6973-60-0 7051-34-5 7210-75-5 7311-34-4 10200-59-6, 2-Thiazolecarboxaldehyde 10203-08-4 10242-08-7 10242-10-1 13349-82-1 13515-93-0 13679-70-4 13679-75-9 13734-41-3 13808-64-5 13889-98-0 13952-84-6, 2-Butanamine 14321-27-8 14610-37-8 15012-74-5 15231-41-1 15433-83-7 16114-47-9 16466-97-0 17249-80-8 17573-92-1 17766-28-8 19524-06-2 20173-04-0 20409-48-7 20980-22-7 20989-17-7 21921-76-6 22078-59-7 22838-58-0 23074-10-4 23095-05-8 23356-96-9 23473-12-3 28250-45-5 29138-64-5 29668-44-8 30084-91-4 32085-88-4 33208-98-9 33240-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

IT 34035-04-6 34036-07-2 34328-61-5 34803-66-2 39515-51-0

39890-42-1 40172-95-0 40357-87-7 42142-52-9 43189-45-3
45121-22-0 45347-82-8, 3-Azetidinol 45521-09-3 50606-58-1
52130-30-0 52480-43-0 52771-21-8 54012-73-6, 3-Piperidinamine
55745-70-5 55745-96-5 56286-73-8 57260-67-0 57260-71-6
57699-45-3 59413-60-4 62348-13-4, 5-Isoxazolecarbonyl chloride
67608-57-5 68820-12-2 68832-13-3 70753-36-5 77873-76-8, 3-**Morpholinecarboxylic** acid 79286-79-6, 3-Pyrrolidinamine
79844-64-7 79852-25-8 80866-91-7 81097-48-5 81661-26-9
94098-56-3 94651-33-9 95201-93-7 101257-87-8 108408-92-0
110013-19-9 119692-41-0 128796-39-4 133712-89-7 135217-58-2
135427-08-6 147701-78-8 180736-67-8 184637-48-7 188816-39-9
189321-66-2 204339-72-0 276702-20-6 276702-25-1 276703-17-4
300582-83-6, 2-**Morpholinecarboxylic** acid 303070-22-6
361393-33-1 413621-62-2 464913-03-9 473730-78-8 473733-45-8
473733-46-9 473733-47-0 473733-48-1 473733-49-2 473733-50-5
473733-51-6 473733-52-7 473733-53-8 473733-54-9 473733-55-0
473736-96-8 473736-98-0 512190-97-5 608537-49-1 608537-54-8
608537-74-2 608538-44-9 612541-21-6 654683-32-6 654683-40-6
654683-69-9 654683-71-3 681509-63-7 681509-64-8 681509-65-9
681509-67-1 681509-68-2 681509-69-3 681509-70-6 681509-71-7
681510-00-9 859838-01-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:988800 CAPLUS
DOCUMENT NUMBER: 124:76317
TITLE: Neuroprotective effects of lamotrigine in global ischemia in gerbils. A histological, in vivo microdialysis and behavioral study
AUTHOR(S): Shuaib, Ashfaq; Mahmood, Rana H.; Wishart, Tom; Kanthan, Rani; Murabit, Mohamed A.; Ijaz, Sadiq; Miyashita, Hiro; Howlett, Wendy
CORPORATE SOURCE: Division of Neurology, Department of Medicine, Royal University Hospital, University of Saskatchewan, Saskatoon, Sask. S7N 0X0, SK, Can.
SOURCE: Brain Research (1995), 702(1,2), 199-206
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Dec 1995
AB A sudden surge in the release of glutamate is currently believed to be an important initiating step in neuronal damage due to an ischemic insult. In this experiment, we tested the efficacy of neuroprotection with lamotrigine, a novel antiepileptic drug that blocks voltage gated sodium channels and inhibits the ischemia-induced release of glutamate in the gerbil forebrain model of cerebral ischemia. The medication was administered 30 min before and 30 min after the insult in two groups of animals. Histol. assessment of neuronal damage was evaluated at 7 and 28 days after the ischemic insult. Animals evaluated at 28 days also underwent behavioral testing. Microdialysis was used in the same model to study the response of ischemia-induced glutamate in saline treated controls vs. animals treated with lamotrigine 20 min before the insult. There was highly significant neuronal protection in animals who were treated with lamotrigine either before or after the insult. Protection was seen both at 7 and 28 days after the insult. Behavioral testing also showed significantly better

recovery in both sets of animals in comparison to the saline-treated group. Microdialysis confirmed a significant attenuation of the ischemia-induced glutamate surge when compared to the saline-treated animals. Our **morphol.**, behavioral and microdialysis expts. show that lamotrigine offers significant neuroprotection from the effects of transient forebrain ischemia in gerbils. Neuroprotection with post-ischemic therapy probably depends on preserving the capacity of the sodium/calcium exchanger to reduce intracellular calcium concns. or persistent 'toxicity' of glutamate in the reperfusion period on the already 'primed' injured neurons. These concepts need further study.

CC 1-11 (Pharmacology)

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective effects of lamotrigine in global ischemia: histol. and behavioral study)

L44 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1010006 CAPLUS
DOCUMENT NUMBER: 144:312050
TITLE: A new approach to the synthesis of lamotrigine and other 3,5-diamino-1,2,4-triazine derivatives
AUTHOR(S): Ulomskii, E. N.; Shestakova, T. S.; Deev, S. L.; Rusinov, V. L.; Chupakhin, O. N.
CORPORATE SOURCE: Ural State Technical University, Yekaterinburg, 620002, Russia
SOURCE: Russian Chemical Bulletin (2005), 54(3), 726-732
CODEN: RCBUEY; ISSN: 1066-5285
PUBLISHER: Springer Science+Business Media, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Sep 2005
AB A new in principle method for the synthesis of 6-aryl(hetaryl)-3,5-diamino-1,2,4-triazines by decomposition of pre-synthesized tetrazolo[1,5-b][1,2,4]triazines was developed. The advantages of this method over traditional methods were demonstrated using the synthesis of a modern antiepileptic preparation lamotrigine, as an example. The crystal structure of 6-phenyltetrazolo[1,5-b][1,2,4]triazin-7-amine is presented [monoclinic, space group P21/c, a 10.935(2), b 6.7330(10), c 13.279(3) Å, β 93.20(3)°, V 976.1(3) Å3, Z 4].
CC 28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 75
IT Bond angle
Bond length
Crystal structure
Hydrogen bond
Molecular structure
(of tetrazolotriazinamine)
IT 879573-90-7P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(mol. and **crystal** structure; preparation of triazinediamines by decomposition of tetrazolotriazines)
IT 6719-24-0P 35857-42-2P 38943-76-9P 38943-80-5P 58848-66-1P
84057-84-1P, Lamotrigine 191872-72-7P 879573-94-1P
879573-95-2P 879573-96-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of triazinediamines by decomposition of tetrazolotriazines)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:823681 CAPLUS
DOCUMENT NUMBER: 143:216704
TITLE: **Crystalline** polymorphs of a CXC-chemokine receptor ligand
INVENTOR(S): Hu, Mengwei; Yu, Younong; Dwyer, Michael; Taveras, Arthur G.; Kim-Meade, Agnes; Yin, Jianguo; Fu, Xiaoyong; Mcallister, Timothy; Zhang, Shuyi; Klopfer, Kevin
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075447	A1	20050818	WO 2005-US3414	20050128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005192345	A1	20050901	US 2005-45772	20050128
PRIORITY APPLN. INFO.:			US 2004-540487P P	20040130

ED Entered STN: 19 Aug 2005
AB The present invention relates to 4 distinct crystalline polymorphs of a monohydrate of 2-hydroxy-N,N-dimethyl-3-[[2-[[1-(5-methyl-2-furanyl)propyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]amino]benzamide. These 4 polymorphic forms, herein referred to as Forms I, II, III and IV are active as a CXC-chemokine receptor ligands. The invention is further directed to formulations, methods of treatment, and processes of synthesis of these polymorphic forms.
IC ICM C07D307-52
ICS A61K031-341; A61P029-00; A61P035-00
CC 63-6 (Pharmaceuticals)
ST **cryst** polymorph CXC chemokine receptor ligand
IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR1; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
(Crohn's disease; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Intestine, disease
(Crohn's; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT GABA receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GABAB; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Antihistamines
(H1; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Antihistamines
(H3; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgE; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Sarcoma
(Kaposi's; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Ear, disease
(Meniere's; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Muscarinic antagonists
(M1; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Muscarinic agonists
(M2; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Muscarinic antagonists
(M3; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Tachykinin receptors
(NK1 antagonists; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Tachykinin receptors
(NK2 antagonists; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ORL1 (opioid receptor-like 1), agonists; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Pancreas, disease
(acute pancreatitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Infection
(acute viral hepatitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Respiratory distress syndrome
(acute; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Respiratory distress syndrome
(adult; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Hepatitis
Liver, disease
(alc.; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Transplant rejection
(allotransplant; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Heart, disease
(angina pectoris; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Dermatitis
(atopic; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Bronchi, disease
(bronchiectasis; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Bronchi, disease
Inflammation
(bronchiolitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Ischemia
(cardiac; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
(carditis, viral; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Ischemia
(cerebral; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Bronchi, disease
Inflammation
(chronic bronchitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Lung, disease
(chronic obstructive pulmonary disease; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Pancreas, disease
(chronic pancreatitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Acne
Alzheimer's disease
Angiogenesis
Angiogenesis inhibitors
Anticoagulants
Anticonvulsants
Antidepressants
Antirheumatic agents
Antitumor agents
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Bronchodilators
Burn
Celiac disease
Common cold
Cough
Cystic fibrosis
Decongestants
Dopamine agonists
Drug delivery systems
Emphysema
Encephalitis
Expectorants
Gout
Hemorrhage
Hepatitis virus
Human
Human herpesvirus
Human immunodeficiency virus 1
Hypercapnia
Immunosuppressants
Inflammation
Ischemia
Leukotriene antagonists
Lupus erythematosus

Malaria
Meningitis
Multiple sclerosis
Neoplasm
Osteoarthritis
Osteoporosis
Pain
Parturition
Platelet aggregation inhibitors
Polymorphism (**crystal**)
Pruritus
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Strain
Thrombolytics
Thrombosis
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Interleukin 10
Interleukin 5
Interleukin 8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Glucocorticoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Allergy
(delayed hypersensitivity; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Eye, disease
(diabetic retinopathy; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Ulcer
(duodenal; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Intestine, disease
(duodenum, ulcer; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Breathing (animal)
(dyspnea; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Esophagus, disease
Inflammation
(esophagitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Lung, disease
(fibrosis; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Ulcer
(gastric; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Gingiva, disease
Inflammation
(gingivitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Kidney, disease
(glomerulonephritis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Tongue, disease
(glossitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Transplant and Transplantation
(graft-vs.-host reaction; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Respiratory system, disease
(hyperresponsiveness; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Hypoxia, animal
(hypoxemia; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Intestine, disease
(inflammatory; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Reperfusion
(injury; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Brain, disease
Heart, disease
(ischemia; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene B4, antagonists; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Eye, disease
(macula, degeneration; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Heart, disease
Inflammation
(myocarditis, viral; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Angiogenesis
(neovascularization, corneal; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Lung, neoplasm
(non-small-cell carcinoma; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Anti-inflammatory agents
(nonsteroidal; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Eye, disease
Inflammation
(ophthalmitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)

IT Inflammation
Periodontium, disease
(periodontitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Dialysis
(peritoneal, continuous ambulatory; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Lung, disease
(pneumonitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Myositis
(polymyositis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Carcinoma
(pulmonary non-small-cell; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Fibrosis
Hypertension
(pulmonary; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Injury
(reperfusion; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Artery, disease
(restenosis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Eye, disease
(retinopathy; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Heart, disease
(right ventricle, hypertrophy; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Hypertrophy
(right ventricular; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Shock (circulatory collapse)
(septic; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation
Respiratory system, disease
(sinusitis, chronic; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Brain, disease
(stroke; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Shock (circulatory collapse)
(toxic shock syndrome; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Injury
(trauma; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Cannabinoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type CB2; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3, antagonists; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Stomach, disease
(ulcer; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Inflammation

Intestine, disease
(ulcerative colitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Blood vessel, disease
Inflammation
(vasculitis; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Hepatitis
(viral, acute; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Breathing (animal)
(wheezing; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT Adrenoceptor agonists
(β2-; **crystalline** polymorphs of CXC-chemokine receptor ligand)
IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-64-1, 2-Propanone, uses 71-23-8, 1-Propanol, uses 75-09-2, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)
IT 862464-58-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)
IT 473727-83-2
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)
IT 50-48-6 53-03-2, Prednisone 53-86-1, Indomethacin 59-05-2, Methotrexate 72-69-5 298-46-4, Carbamazepin 378-44-9, Betamethasone 446-86-6 599-79-1, Sulfasalazine 9005-49-6, Heparin, biological studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1, Naproxen 36322-90-4, Piroxicam 60142-96-3, Gabapentin 65271-80-9 71125-38-7, Meloxicam 75706-12-6, Leflunimide 79217-60-0, Cyclosporin **84057-84-1**, Lamotrigine 105857-23-6, Alteplase 139639-23-9, Tissue plasminogen activator 143653-53-6, Abciximab 147245-92-9, Glatiramer acetate 148553-50-8, PreGabalin 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170277-31-3, Infliximab 181695-72-7, Valdecoxib 185243-69-0, Etanercept 188627-80-7, Eftifibatide 191588-94-0, Tenecteplase 202409-33-4, Etoricoxib 331731-18-1, Adalimumab
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**crystalline** polymorphs of CXC-chemokine receptor ligand)
IT 9001-84-7, Phospholipase A2 9001-87-0, Phospholipase D 9004-06-2, Elastase 9025-82-5, Phosphodiesterase 9036-21-9, Phosphodiesterase 4 39391-18-9 80619-02-9 141907-41-7 165245-96-5, P38 Kinase 329900-75-6 329967-85-3, Cyclooxygenase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **crystalline** polymorphs of CXC-chemokine receptor ligand)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:799572 CAPLUS

DOCUMENT NUMBER: 141:282838
TITLE: Novel **crystalline** forms of lamotrigine
INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari; Subash, Chander Reddy Kesireddy
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083191	A1	20040930	WO 2003-IN57	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003217437	A1	20041011	AU 2003-217437	20030317
US 2005119265	A1	20050602	US 2003-508099	20030317
EP 1603889	A1	20051214	EP 2003-712623	20030317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: WO 2003-IN57 A 20030317

ED Entered STN: 30 Sep 2004

AB The present invention relates to novel crystalline forms of lamotrigine, to processes for their preparation and pharmaceutical compns. containing them. A process for preparation of crystalline forms of lamotrigine comprises steps of (i) dissolving lamotrigine in a solvent, (ii) maintaining the solvent at certain temperature for certain time, and (iii) filtering the crystal form solid. For example, 10 g of lamotrigine was added to 100 mL of dioxane, maintained at 50° to 55° for 60 min, cooled to 25° and maintained at this temperature for 2 h. The solid was separated by filtration to give 8.5 g of Form II lamotrigine.

IC ICM C07D253-075
ICS A61K031-53

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 75

ST lamotrigine polymorphism **cryst** form prepn delivery system

IT Drug delivery systems
Polymorphism (**crystal**)
(preparation of stable **crystalline** forms of lamotrigine for delivery systems)

IT Esters, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(solvents; preparation of stable **crystalline** forms of lamotrigine for delivery systems)

IT **84057-84-1**, Lamotrigine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP

(Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of stable **crystalline** forms of lamotrigine for delivery systems)

IT 67-66-3, Chloroform, processes 68-12-2, Dimethylformamide, processes 79-20-9, Methyl acetate 108-21-4, Isopropyl acetate 109-94-4, Ethyl formate 123-91-1, Dioxane, processes 141-78-6, Ethyl acetate, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(preparation of stable **crystalline** forms of lamotrigine for delivery systems)

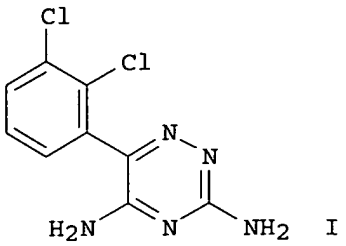
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:421470 CAPLUS
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of **crystalline** lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A1	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-15608 A 20030703
OTHER SOURCE(S): CASREACT 141:7119
ED Entered STN: 26 May 2004
GI



I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.

IC ICM C07D253-075
ICS A61K031-53; A61P025-08

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))

ST anhyd lamotrigine prepn; **cryst** lamotrigine monohydrate prepn; cyclization dichlorophenylguanidinyliminoacetonitrile; condensation dichlorobenzoyl cyanide aminoguanidine

IT Acids, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(inorg.; preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT Condensation reaction
Cyclization
Green chemistry
(preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT Schiff bases
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT **84057-84-1P**, Lamotrigine **375347-20-9P**, Lamotrigine monohydrate
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(**X-ray diffraction** anal.; preparation of

crystalline lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT 2905-60-4P, 2,3-Dichlorobenzoyl chloride 77668-42-9P, 2,3-Dichlorobenzoyl cyanide 84689-20-3P, (2,3-Dichlorophenyl)(guanidinylimino)acetonitrile
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT 50-45-3, 2,3-Dichlorobenzoic acid 544-92-3, Copper cyanide 1068-42-4, Aminoguanidine sulfate 1937-19-5, Aminoguanidine hydrochloride 2582-30-1, Aminoguanidine bicarbonate 10308-82-4, Aminoguanidine nitrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT 7647-01-0, Hydrochloric acid, reactions 7664-38-2, Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions 7697-37-2, Nitric acid, reactions 10035-10-6, Hydrobromic acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropyl alcohol, uses 67-68-5, Dimethyl sulfoxide, uses 68-12-2, Dimethylformamide, uses 71-23-8, n-Propanol, uses 71-36-3, n-Butanol, uses 75-05-8, Acetonitrile, uses 75-65-0, tert-Butanol, uses 111-46-6, Diethylene glycol, uses 123-91-1, 1,4-Dioxane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of **crystalline** lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:267313 CAPLUS
DOCUMENT NUMBER: 140:303705
TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate
INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2498761	AA	20040401	CA 2003-2498761	20030918
AU 2003267676	A1	20040408	AU 2003-267676	20030918
EP 1539720	A1	20050615	EP 2003-748368	20030918

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	HU 2002-3114	A	20020920
	WO 2003-HU72	W	20030918

OTHER SOURCE(S): CASREACT 140:303705
ED Entered STN: 01 Apr 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is prepared by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).
IC ICM C07D253-06
ICS C07C281-16
CC 28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45
IT **Crystallization**
(in the preparation of high-purity lamotrigine)
IT **84057-84-1P**, Lamotrigine
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:499101 CAPLUS
DOCUMENT NUMBER: 136:5580
TITLE: Hydrogen bonding patterns in 3,5-diamino-6-aryl triazines
AUTHOR(S): Kubicki, M.; Codding, P. W.
CORPORATE SOURCE: Faculty of Chemistry, Laboratory of Crystallography, Adam Mickiewicz University, Poznan, 60-780, Pol.
SOURCE: Journal of Molecular Structure (2001), 570(1-3), 53-60
CODEN: JMOSB4; ISSN: 0022-2860
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 11 Jul 2001
AB The crystal structure of two related 1,2,4-triazine derivs.,

C9H7N5Cl2·H2O (I) and C12H14N5Cl2+·CH3SO3-·H2O (II) that have different biol. effects, have been determined Lamotrigine (Lamictal), I, is a novel anticonvulsant and BWA256C, II, is a class 1 antiarrythmic drug. The dihedral angles between the least-squares planes of almost exactly planar Ph and triazine rings are 76.42(6) and 76.08(6)°, for compds. I and II, resp. In II, protonation takes place at the iminium nitrogen atom, thus suggesting the importance of resonance through the triazine ring. This resonance is also confirmed by the pattern of bond lengths and angles. Extensive networks of hydrogen bonds, in which all mol. species are involved, rule the crystal packing in both compds. The anal. of hydrogen bond networks in other 3,5-diamino-6-aryl derivs. suggests that there is a strong influence of co-crystallizing solvent mol. on the nature of resulting hydrogen bond topol.

CC 22-3 (Physical Organic Chemistry)
Section cross-reference(s): 1, 28, 75

ST lamictal hydrogen bonding **crystallog** mol structure

IT Antiarrhythmics
Anticonvulsants
Crystal structure
Hydrogen bond
Molecular structure
(hydrogen bonding patterns in **crystal** structure of 3,5-diamino-6-aryl triazines)

IT 374938-50-8 **375347-20-9**, Lamotrigine hydrate
RL: PRP (Properties)
(**crystal** structure; hydrogen bonding patterns in **crystal** structure of 3,5-diamino-6-aryl triazines)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

ED Entered STN: 11 May 2001

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IC ICM C12Q001-68
ICS G01N033-50

CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 7, 13, 15

IT **Crystallins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ζ- **crystallins**; methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT 3778-73-2, Iphosphamide 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 4499-40-5, Oxtriphylline, biological studies 4618-18-2, Lactulose 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin 5051-62-7, Guanabenz 5543-57-7, (s)-Warfarin 5633-20-5, Oxybutynin 5786-21-0, Clozapine 6190-39-2, Dihydroergotamine mesylate 6493-05-6, Pentoxifylline 6621-47-2, Perhexiline 7020-55-5, Clidinium 7235-40-7, Beta carotene 7261-97-4, Dantrolene 7416-34-4, Molindone 7439-93-2, Lithium, biological studies 7447-40-7, Potassium chloride, biological studies 7481-89-2, Zalcitabine 7487-88-9, Magnesium sulfate, biological studies 7648-98-8, Ambenonium 7681-11-0, Potassium iodide, biological studies 7681-93-8, Natamycin 7683-59-2, Isoproterenol 8029-99-0, Paregoric 8049-47-6, Pancreatin 8050-81-5, Simethicone 8063-07-8, Kanamycin 8067-24-1, Ergoloid mesylates 9001-27-8, BLood-coagulation factor VIII 9001-75-6, Pepsin 9004-10-8, Insulin, biological studies 9004-67-5, Methyl cellulose 9005-49-6, Enoxaparin, biological studies 9007-92-5, Glucagon, biological studies 9039-53-6, Urokinase 9046-56-4, Ancrod 10118-90-8, Minocycline 10238-21-8, Glyburide 10262-69-8, Maprotiline 10540-29-1, Tamoxifen 11041-12-6, Cholestyramine 11056-06-7, Bleomycin 11111-12-9, Cephalosporin 12174-11-7, Attapulgite 12244-57-4, Gold sodium thiomalate 12650-69-0, Mupirocin 12794-10-4D, Benzodiazepine, derivs. 13010-47-4, Lomustine 13292-46-1, Rifampin 13311-84-7, Flutamide 13392-28-4, Rimantadine 13647-35-3, Trilostane 14028-44-5, Amoxapine 14124-50-6 14611-51-9, Selegiline 14769-73-4, Levamisole 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate 15301-69-6, Flavoxate 15307-86-5, Diclofenac 15663-27-1, Cisplatin 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 16051-77-7, Isosorbide mononitrate 16068-46-5, Potassium phosphate 16110-51-3, Cromolyn 16590-41-3, Naltrexone 16679-58-6, Desmopressin 17230-88-5, Danazol 17784-12-2, Sulfacytine 18323-44-9, Clindamycin 18559-94-9, Albuterol 18883-66-4, Streptozocin 19216-56-9, Prazosin 19794-93-5,

Trazodone 20537-88-6, Amifostine 20830-75-5, Digoxin 20830-81-3, Daunomycin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 22232-71-9, Mazindol 23031-32-5, Terbutaline sulfate 23214-92-8, Doxorubicin 23288-49-5, Probucol 25322-68-3, Polyethylene glycol 25451-15-4, Felbamate 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26652-09-5, Ritodrine 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8, Timolol 27203-92-5, Tramadol 27262-47-1, Levobupivacaine 27686-84-6, Masoprocol 28395-03-1, Bumetanide 28657-80-9, Cinoxacin 28782-42-5, Difenoxin 28860-95-9, Carbidopa 28911-01-5, Triazolam 28981-97-7, Alprazolam 29094-61-9, Glipizide 29110-47-2, Guanfacine 29122-68-7, Atenolol 30516-87-1, Zidovudine 31441-78-8, Mercaptopurine 31677-93-7, Bupropion hydrochloride 31828-71-4, Mexiletine 31883-05-3, Moricizine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34089-81-1, Sodium ferric gluconate 35189-28-7, Norgestimate 36322-90-4, Piroxicam 36505-84-7, Buspirone 36791-04-5, Ribavirin 38304-91-5, Minoxidil 40180-04-9, Tienilic acid 40580-59-4, Guanadrel 41575-94-4, Carboplatin 41708-72-9, Tocainide 42399-41-7, Diltiazem 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 50679-08-8, Terfenadine 50925-79-6, Colestipol 50972-17-3, Bacampicillin 51022-71-0, Nabilone 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol 51481-61-9, Cimetidine 53179-11-6, Loperamide 53230-10-7, Mefloquine 53608-75-6, Pancrelipase 53714-56-0, Leuprolide 53994-73-3, Cefaclor 54024-22-5, Desogestrel 54063-53-5, Propafenone 54143-56-5, Flecainide acetate 54182-58-0, Sucralfate 54350-48-0, Etretinate 54573-75-0, Doxercalciferol 54910-89-3, Fluoxetine 55142-85-3, Ticlopidine 55268-75-2, Cefuroxime 55985-32-5, Nicardipine 56420-45-2, Epirubicin 58001-44-8 58581-89-8, Azelastine 59122-46-2, Misoprostol 59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporine A 60142-96-3, Gabapentin 60205-81-4, Ipratropium 61489-71-2, Menotropin 61718-82-9, Fluvoxamine maleate 61869-08-7, Paroxetine 62571-86-2, Captopril 63585-09-1, Foscarnet sodium 63590-64-7, Terazosin 64952-97-2, Latamoxef 65141-46-0, Nicorandil 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66104-22-1, Pergolide 66357-35-5, Ranitidine 66376-36-1, Alendronate 67227-57-0, Fenoldopam mesylate 68475-42-3, Anagrelide 68844-77-9, Astemizole 69049-73-6, Nedocromil 69123-98-4, Fialuridine 69655-05-6, Didanosine 70359-46-5, Brominide tartrate 70989-04-7, S-Mephenytoin 71320-77-9, Moclobemide 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3, Carvedilol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8, Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6, Leflunomide 75847-73-3, Enalapril 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76568-02-0, Flosequinan 76584-70-8 76824-35-6, Famotidine 76932-56-4, Nafarelin 76963-41-2, Nizatidine 78110-38-0, Aztreonam 78628-80-5, Terbinafine hydrochloride 79516-68-0, Levocabastine 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 80125-14-0, Remoxipride 80474-14-2, Fluticasone propionate 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81669-57-0, Anistreplase 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 82834-16-0, Perindopril 83366-66-9, Nefazodone 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin **84057-84-1**, Lamotrigine 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85441-61-8, Quinapril 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88040-23-7, Cefepime 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89778-26-7, Toremifene 90566-53-3, Fluticasone 91714-94-2, Bromfenac

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical agent

from gene expression profile)

L44 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:12098 CAPLUS
DOCUMENT NUMBER: 132:130210
TITLE: Structure of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate solvate (lamotrigine isethionate)
AUTHOR(S): Potter, Brian; Palmer, Rex A.; Withnall, Robert; Leach, Michael J.; Chowdhry, Babur Z.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(6), 701-706
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Jan 2000
AB The crystal and mol. structure of lamotrigine isethionate was determined by direct methods. The compound crystallizes in the tetragonal space group I41/a, with a 19.684(5), c 16.557(5) Å; Z = 16, dc = 1.579; R = 0.0532, Rw = 0.1317 for 2041 reflections. Atomic coordinates are given. The isethionate moiety forms multiple H bonds to the lamotrigine nucleus, three from one isethionate, two from a symmetry related isethionate and a further two from two different symmetry related mols. Protonation of N(2') in the triazine ring, not observed in the native lamotrigine structure is presumably associated with the interaction of the isethionate moiety. Both rings in the lamotrigine moiety are essentially planar, with a dihedral angle of 66.08(7)° compared to 80.70° in native lamotrigine. The connecting bond length C(1)-C(6') 1.493(3) Å also correlates well with values in related compds. (1.480(3) Å) in the native structures.
CC 75-8 (Crystallography and Liquid Crystals)
Section cross-reference(s): 28
ST mol structure lamotrigine isethionate; **crystal** structure lamotrigine isethionate; hydrogen bond lamotrigine isethionate; protonation lamotrigine isethionate
IT **Crystal** structure
Molecular structure
(of lamotrigine isethionate)
IT **113170-86-8**, Lamotrigine isethionate
RL: PRP (Properties)
(**crystal** structure of)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:616102 CAPLUS
DOCUMENT NUMBER: 125:256936
TITLE: Moisture-Dependent **Crystallization** of Amorphous Lamotrigine Mesylate
AUTHOR(S): Schmitt, E.; Davis, C. W.; Long, S. T.
CORPORATE SOURCE: Glaxo Wellcome Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Pharmaceutical Sciences (1996), 85(11), 1215-1219
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 17 Oct 1996
AB A com. available computer-controlled vacuum moisture balance was used for determining moisture sorption isotherms of freeze-dried and spray-dried lamotrigine mesylate and freeze-dried drug product containing mannitol. The presence or absence of desorption hysteresis and the characteristics of the weight-vs.-time profile as a sample was exposed to a defined relative humidity ramp were sensitive indicators of moisture-induced crystallization Combination of the moisture sorption data with polarized light microscopy, DSC, and **x-ray** powder **diffraction** provided qual. verification of the crystallization with <50 mg of sample. The normalized water loss during crystallization was used to detect as little as 2% amorphous content in phys. mixts. of amorphous and crystalline lamotrigine mesylate. Moisture sorption, water plasticization, and crystallization properties of amorphous forms prepared by spray drying and freeze drying were nearly identical. Cofreeze-drying lamotrigine mesylate with D-mannitol resulted in a mixture of amorphous lamotrigine mesylate with properties similar to those of spray-dried or freeze-dried materials and crystalline D-mannitol. The amount of water needed for crystallization over a time scale observable in the moisture balance was considerably more than the amount needed to lower the glass transition temperature of the sample to the operating temperature of the instrument. This result illustrated the importance of time scale effects in determining critical moisture levels for crystallization from the amorphous state.
CC 63-5 (Pharmaceuticals)
ST lamotrigine mesylate **crystn** moisture
IT **Crystallization**
Freeze drying
Glass temperature and transition
Sorption
(moisture-dependent **crystallization** of amorphous lamotrigine mesylate)
IT Drying
(spray, moisture-dependent **crystallization** of amorphous lamotrigine mesylate)
IT **181362-54-9**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(moisture-dependent **crystallization** of amorphous lamotrigine mesylate)
IT 69-65-8, D-Mannitol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(moisture-dependent **crystallization** of amorphous lamotrigine mesylate)

L44 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:126056 CAPLUS
DOCUMENT NUMBER: 110:126056
TITLE: Structure of lamotrigine methanol solvate: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-methanol, a novel anticonvulsant drug
AUTHOR(S): Janes, Robert W.; Lisgarten, John N.; Palmer, Rex A.
CORPORATE SOURCE: Birkbeck Coll., Univ. London, London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1989), C45(1), 129-32
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Apr 1989
AB The title compound is monoclinic, space group P21/n, with a 15.456(3), b

11.736(2), c 7.300(3) Å, and β 94.417(3)°; Z = 4 for dc = 1.449. The final R = 0.055 for 2444 reflections. Atomic coordinates are given. The Ph and triazine aromatic rings make a dihedral angle of 80.6(9)° with each other. The bond linking the 2 rings is 1.480(3) Å. The structure is stabilized by a network of H bonds involving amino and ring N atoms, one of the Cl atoms, and the MeOH of crystallization

CC 75-8 (Crystallography and Liquid Crystals)
Section cross-reference(s): 1, 28

IT **Crystal** structure
Molecular structure
(of diamino(dichlorophenyl)triazine-methanol solvate)

IT **119441-74-6**
RL: PRP (Properties)
(**crystal** structure of)

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L48 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:875073 CAPLUS
DOCUMENT NUMBER: 139:354488
TITLE: Pharmaceutical composition containing lamotrigine particles of defined morphology
INVENTOR(S): **Aronhime, Judith**; **Samburski, Guy**
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090693	A2	20031106	WO 2003-US13002	20030423
WO 2003090693	A3	20040108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2483103	AA	20031106	CA 2003-2483103	20030423
AU 2003234240	A1	20031110	AU 2003-234240	20030423
EP 1496864	A2	20050119	EP 2003-728552	20030423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005238724	A1	20051027	US 2004-511987	20041021
PRIORITY APPLN. INFO.:			US 2002-374923P P	20020423
			WO 2003-US13002 W	20030423

L48 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:676002 CAPLUS
DOCUMENT NUMBER: 137:222039
TITLE: New crystal forms of lamotrigine and processes for their preparations
INVENTOR(S): Garti, Nissim; Berkovich, Yana; Dolitzky, Ben-Zion; **Aronhime, Judith**; Singer, Claude; Lieberman, Anita; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     WO 2002068398          A1     20020906     WO 2002-US6160          20020227
     WO 2002068398          C2     20021121
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             TJ, TM
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     CA 2439468             AA     20020906     CA 2002-2439468         20020227
     US 2003018030          A1     20030123     US 2002-86157           20020227
     US 6861426             B2     20050301
     EP 1390355             A2     20040225     EP 2002-706471          20020227
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2004526714          T2     20040902     JP 2002-567912          20020227
     US 2005171107          A1     20050804     US 2005-45355           20050131
PRIORITY APPLN. INFO.:                           US 2001-271688P      P  20010227
                                                 US 2002-86157        A1 20020227
                                                 WO 2002-US6160       W  20020227
REFERENCE COUNT:          2      THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    3.86        8.87

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:13:14 ON 17 JUL 2006
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